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The Journal of
Obstetrics and Gynaecology of the British Empire

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THE VALUE OF CYTOLOGY IN GYNAECOLOGY

BY

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IN 1951 we were asked by the Royal College of Obstetricians and Gynaecologists to set up a cytology laboratory and to report on the value of cytology in gynaecological practice.

The detection of cancer cells in vaginal smears was of course well established by 1951 in many centres throughout the world—especially in the United States (Papanicolaou, 1928; Meigs *et al.*, 1945; Achenbach, Johnstone and Hertig, 1951), Canada (Ayre, 1947) and also in a few centres in Britain (Dudgeon and Patrick, 1925; Wachtel and Plester, 1952; Anderson *et al.*, 1953; Osborn, 1953). Many gynaecologists, however, were anxious to know how many cases of cancer a cytologist would discover which would not be recognized by the usual clinical methods employed in their own out-patient departments. This information would help them to decide whether or not this expensive and time-consuming work would be worth while. The question which required an answer was this: is cytology obligatory in gynaecological practice?

From 1952 until now cytological investigations have been carried out on over 5,000 patients and the work continues. This first report concerns the establishment of cytology in our clinical unit and the findings on 3,337 smears from the first 2,250 patients. Many patients had repeated smears taken for various reasons.

THE ESTABLISHMENT OF CYTOLOGY IN THE UNIT

In 1952, with a grant from the United Birmingham Hospitals Endowment Fund and with the help and encouragement of A. T. Hertig, our senior technician in charge of the gynaecological laboratory (M.E.A.) was sent for 7-months training under Mrs. Rachel Achenbach and Mrs. Graham (Boston) and later with G. N. Papanicolaou (New York) and J. E. Ayre (Miami). With her help it was then possible to establish a cytology laboratory within the Department and to commence training other technicians.

We had to decide at the outset whether or not to adopt the system used in many centres in the United States of America where the initial screening of smears is carried out by personnel whose duties are: (*a*) to report smears as free from cells resembling cancer—the negative smear, and (*b*) to refer suspicious smears to an expert who is responsible for signing the report. The alternative was to make the cytologist, and in time her trained personnel, responsible for

their own reports and this was the policy we adopted. There is no medically qualified cytologist in the Department.

Our technicians varied in their aptitude but in general not less than 6 months was necessary for them to become efficient. They then became responsible for their own reports on a smear. In our experience, attendance at Out-patients gave the trainees a sense of being members of the clinical team with definite responsibility for the diagnosis and ultimately for the care of patients. By putting full responsibility for "cell-recognition" and cytological opinion on our cytologists we have deliberately avoided training "screeners".

Material for smears was obtained by the vaginal aspiration technique in the hands of the cytologist or her trainees. This method has the advantage over Ayre's scraping of the portio vaginalis in that the vaginal smear, the taking of which does not require a speculum, contains many cells from the endometrium and endocervix as well as cells from the portio vaginalis. If the smear was unsatisfactory a further smear was taken either in Out-patients or in the wards by the cytologist. Except where stated, this report concerns the findings on the first vaginal aspiration, although on occasions, when the routine speculum examination was being carried out by the clinician a "scrape" was taken for interest from the portio.

Clinical Material

The experiment was limited to cases under the care of the Professorial Unit and vaginal smears were taken from patients attending an ordinary gynaecological out-patient department not specially involved in the diagnosis of cancer. All clinical records were made by H. C. McLaren (Professor), M. J. D. Noble (First Assistant), R. B. Parker (Clinical Lecturer) and very occasionally by our registrars, D. L. Phillips and B. J. Murphy. Dr. C. W. Taylor (Director of Pathology) was responsible for all the pathological studies.

Method

At the outset only one clinic could be screened but with the completion of training of other technicians all three out-patient sessions in the unit were included. It became obvious after we had screened 800 patients that, to enable us to make the strictest assessment of the value of the technique, we had to design for our clinical team a special case-sheet with the specific object of making the clinician state whether each patient was or was not suspected of having cancer. This case-sheet was supplementary to the ordinary out-patient notes but, with practice, the clinical team could complete it in 2 or 3 minutes. As will be seen it required the clinician to make enquiry concerning intermenstrual and post-coital bleeding in every case, while every cervix had to be inspected. About half of our cases were subjected to the special questionnaire, viz., 1,030 out of 2,290.

Name: Age: Single / Widow / Married (years)

Complaints: 1. 2. 3. 4.

Menstrual History: Menarche: Last menstrual period: Cycle: Bleeding between periods:

Obstetric History: No. of children: (birth dates) (Caesarean) Miscarriages: (maturity dates)

Leucorrhoea: Onset: Pads/day: Type: mucus, yellow, white, blood stained?

Drugs: Stilboestrol, Amphetamine, Menopax, pessaries, others.

If married: Post-coital bleeding: Yes: Duration. No:

Previous Illness and/or Operations:

Deaths in family:

Examination

General: Healthy, obese, thin, etc.

Gynaecological findings: Vulva: normal / abnormal (details)

Vaginal discharge: Normal, white, blood stained or (give details).

Bimanual findings: Adnexa: Body: normal. abnormal (details).

Cervix: Normal.
Abnormal (details).
Speculum Examination: (*a*) not possible:
(*b*) findings:

(Diagram of portio vaginalis for word picture)

Erosion: absent.
Erosion: present (shade in diagram).
Size: (tiny area, moderate, large).
Fleshy:
Flat:
Friable:
Firm:
Contact bleeding: (bled with wool, wooden scraper or swab).
Mucus: Amount:
Type: clear, fluid, tenacious, blood stained (menses?).
Other remarks: (polyp, etc.)
Clinical Diagnosis: 1.
2.
3.
Cancer of Body: Suspected (reason).
Not suspected.
Cancer of Cervix: Suspected (reason).
Not suspected.
Disposal: D. and C.
Biopsy of cervix.

In view of the differing opinions on what gynaecologists regard as suspicious findings at the portio vaginalis we should state that our clinical team came to an agreement. For instance, split cervices from old obstetric lacerations were described in detail and from a clinical point of view recorded as being innocent provided there were no relevant symptoms. So-called clinical erosions (present in as many as 20 per cent of cases) were recorded in diagrammatic form on the special case-sheet and were regarded as clinically innocent. In fact, the clinical team worked on the assumption that erosions of the cervix are so common that they are physiological and being asymptomatic in the large majority of cases required neither investigation nor treatment. If, however, the erosion bled actively and much more than is usual on palpation or on gentle mopping with dry wool the condition was regarded with suspicion. (We should state that our Ingleby Lecturer in the University for 1954, Dr. Paul Younge, has been led by his experience to regard not only the vascular type of erosion but all erosions with suspicion so that in this the clinical team are not working in accord with his teaching.) (Younge, Hertig and Armstrong, 1949.)

Twenty-three patients with suspicious cervices were admitted for investigation. One unhealed pessary ulcer obviously required biopsy and carcinoma was confirmed but of the remainder not one proved to have carcinoma or carcinoma *in situ*.

Post-coital bleeding presented in 9 out of 1,206 ordinary out-patients (0·75 per cent) but in the series screened by the "exclude cancer" case-sheet the incidence was 23 out of 1,032 (2·2 per cent). Further clinical findings are summarized in Table I.

The special case-sheet to exclude cancer did not, in fact, raise our diagnostic success in carcinoma or carcinoma *in situ*. The precise definition of a true positive smear or "pick-up" to be accredited to cytology was simplified by its use and this was one of the chief objects of our work in assessing the value of cytology in gynaecology.

We define a "pick-up" as follows:

(*a*) If a patient after consultation in the clinic was referred back to her doctor but her smear contained malignant cells, she was recalled; a "pick-up" was awarded if

TABLE I
Patients Under Suspicion

	Totals	Post-menopausal Haemorrhage		Post-coital Bleeding		Climacteric Uterine Haemorrhage	Intermenstrual Loss	Blood-stained Discharge	Suspicious Cervix	Follow-up After Cancer Therapy	Carcinoma Vulva	Carcinoma Vagina
		No.	Per cent	No.	Per cent							
Ordinary Out-patients	154	80	52	9	5·8	10	3		8	37	6	1
Out-patients with special questionnaire aimed at the exclusion of cancer	120	60	50	23	19	7	7	1	15	4	3	

274 out-patients (12 per cent) were considered to be suspect or under suspicion. The effect of set questions is obvious, e.g., in post-coital bleeding which increased from 6 per cent to 19 per cent of all "suspected" patients (or 0·75 per cent of all gynaecological out-patients).

carcinoma or carcinoma *in situ* was confirmed.

(*b*) If routine investigation of a patient with post-menopausal bleeding failed to reveal carcinoma but the smear continued to be positive—if re-examination revealed carcinoma, a "pick-up" was awarded.

Correlation of Clinical and Cytological Findings

Since one of our objects was to obtain an exact knowledge of the accuracy of cytology in gynaecological practice a close liaison between the clinician and the cytologist was essential. Thus, every patient with a positive smear, irrespective of symptoms, was admitted for investigation which consisted of curettage of the uterine body and endocervix and a ring biopsy of the cervix. Adequate tissue was obtained by including in the ring biopsy the squamo-columnar junction and much of the lower cervical canal. An ordinary Bard-Parker knife was used.

The accuracy of cytology is weighed against the histological report. In this experiment all histology was reported by one of us (C.W.T.) independently of the cytology report.

The histological findings in the cervical tissues examined have been classified as:

1. Benign.
2. Carcinoma.
3. Carcinoma *in situ* (*a*) typical.
   (*b*) equivocal.

Provided the histologist is familiar with the physiological variations of the cervical epithelium, the diagnosis of a benign lesion, such as erosion, usually offers little difficulty. The same can be said of definitely invasive carcinoma.

A histological diagnosis of carcinoma *in situ*, however, is often difficult and depends on personal interpretation. Many cases fall within the strict criterion—the entire thickness of the surface epithelium is replaced by malignant cells; these we have called typical carcinoma *in situ*. On the other hand, abnormal cellular hyperplasia, though similar in nature, may show maturation of the superficial squamae. Such a lesion, though not falling into the strict criterion of carcinoma *in situ*, may strongly suggest malignant intra-epithelial change—sometimes more so than the typical lesion. To these cases we have applied the term *equivocal carcinoma in situ*. This epithelial change is quite distinct from simple stratification and epidermization which themselves may give rise to bizarre patterns but are recognized as benign metaplasia by the experienced pathologist. Galvin, Jones and Te Linde (1955) have described three grades of basal cell hyperplasia of the cervical epithelium and conclude that the third stage may progress to carcinoma *in situ*, although regression can occur (Peckham *et al.*, 1954). One of us has seen examples that we refer to as equivocal carcinoma *in situ* merge into typical carcinoma *in situ*.

The need for some uniformity in the interpretation of atypical epithelial change in the cervix is apparent to anyone involved in this problem. We feel justified in the present experiment in including the cases of equivocal carcinoma *in situ* (though we dislike the term) as probable precursors of carcinoma. They are being carefully followed up.

Involvement of the cervical mucous glands may be seen in both typical and equivocal types of carcinoma *in situ*. We have not regarded this as evidence of invasion. A diagnosis of carcinoma supervening on carcinoma *in situ* is only made "where the carcinoma has penetrated the basal membrane and is independently growing in the stromal tissue" (Kottmeier, 1955).

With regard to the study of ring biopsy material adequate tissue was necessary and serial sectioning carried out. Finally, it is well to remember in considering a pathological report that the presence of carcinoma *in situ* in one portion does not exclude invasive carcinoma elsewhere in the cervix.

Terms Used in Cytology

The reporting of smears as positive, suspicious or negative is adequate but we have a classification based on Papanicolaou's grading, viz.:

Grade I Absence of atypical or abnormal cells.

Grade II Atypical findings but no evidence of malignancy.

Grade III Presence of cells suspicious of malignancy.

Grade IV Presence of cells suggestive of malignancy.

Grade V Presence of cells conclusive of malignancy.

Except where clearly stated in the case reports this assay of the value of cytology concerns the first vaginal smear. Suspicious smears were repeated whenever possible.

Clinical Material

Total number of patients screened	2,290
Patients with inadequate notes ..	54
Patients with no smear	40
Patients with smears and adequate notes	2,196

RESULTS

(a) *Cervix*

Carcinoma of portio vaginalis ..	31	34
Carcinoma of endocervix ..	3	

The cytologist recognized cancer cells in 33 out of 34 vaginal smears from carcinoma of the cervix. The single error was obvious on re-examination of the smear.

(b) *Corpus*

Carcinoma of corpus	14
Sarcoma of corpus	2

The cytologist recognized cancer cells in 12.

(c) *Carcinoma* in situ:

Typical	5

The cytologist recognized malignant cells in 4. One was diagnosed as a result of a biopsy taken from an apparently simple erosion.

Equivocal	4

The cytologist recognized malignant cells in all 4.

A false positive smear is defined as a positive cytological report where routine curettage and ring biopsy of the cervix, or histology of the uterus removed at hysterectomy, fail to reveal either uterine carcinoma or carcinoma *in situ*.

Total number of false positive smears	6
Total number of positive smears	64
Incidence in 2,250 cases; 3,337 smears	0·26 per cent
Incidence in 64 positive smears	9 per cent

There were also 5 positive smears without complete pathological studies and we have included this group as false positive smears; so that, in all, 11 out of 64 positive smears were false, an incidence of 17 per cent.

From a clinical point of view a false positive smear means that unnecessarily an anaesthetic and full investigation including a ring biopsy is required. A high incidence of false positive smears would be vexatious but, in fact, about 1 in over 200 of all our patients is not considered to be unduly high.

A false negative smear is defined as a negative cytological report where subsequent investigations revealed the presence of carcinoma or carcinoma *in situ*. In this series there were 6 false negative smears (10 per cent of all malignant cases or 0·26 per cent of all cases).

False Negative Smears

Case	Smear	Disease	Remarks
1	Unsatisfactory.	Carcinoma of corpus.	No repeat taken.
2	Unsatisfactory.	Carcinoma of corpus.	No repeat taken.
3	Suspicious III.	Carcinoma of corpus.	No repeat taken.
4	Smear II. (Normal)	Sarcoma of corpus.	No repeat smear.
5	Smear II. (Normal)	Carcinoma *in situ*.	No cancer cells on review of slide.
6	Smear II. (Normal)	Carcinoma of cervix.	Error: on review smear positive (IV).

Suspicious smears (*Grade III*) are defined as smears where the cytological appearance, although suspicious, does not warrant a "diagnosis" of malignancy but warrants further study in subsequent smears. In this series the incidence of such "suspicious—please repeat" smears was 128 or 5·7 per cent.

Of our 128 suspicious smears either histology was available or further clinical and cytological studies were undertaken in 99 without evidence of malignancy. We found that the number of suspicious smears rapidly decreased as the

cytologist gained in experience. In summary:

Total number of cases	2,250
Total number of suspicious smears (Grade III)	128 (5·7 per cent)
Of 128 smears graded as III and finally diagnosed as innocent (Grade II)	99
Number finally diagnosed (IV "cancer cells") and malignancy confirmed	10
Number not available for further study	19

CASES PICKED UP BY CYTOLOGY

Carcinoma of portio vaginalis ..	1
Carcinoma corporis	1
Typical carcinoma *in situ*, cervix	4
Equivocal carcinoma *in situ* ..	4

Cytology was responsible for leading us to the diagnosis of 10 cases in all, but only 2 cases of invasive carcinoma in 2,250 out-patients. To our 4 examples of typical carcinoma *in situ* can be added a further case diagnosed as a result of a ring biopsy from what appeared to be a somewhat vascular erosion. This chance diagnosis of carcinoma *in situ* emphasizes a point made by Isbell *et al.* (1947) in regard to the total incidence of this interesting condition which is not known but is generally stated to be higher than 8 in 2,250 gynaecological out-patients (Nieburgs, 1951; Ayre, 1947, 1954; Graham, 1950; Mackenzie *et al.*, 1948).

As stated before, for the diagnosis of carcinoma *in situ* the careful questions and examination recorded in the special case-sheet would not, considered in retrospect, appear to have helped us at all.

We feel that the key to this assay of cytology is the 10 cases discovered by the method. These are summarized:

Case 1: Carcinoma of Cervix

Mrs. Y., aged 34, para-2, reported early in our series with vaginal discharge and menorrhagia. She was admitted for diagnostic curettage. The cervix was parous and no biopsy was considered necessary from a clinical point of view. The first smear taken in Out-patients was positive (IV) but no ring biopsy was taken; curettings showed metropathia. At follow-up 3 months later she was in better health and symptom-free; her smear was then only suspicious. Although given a further appointment the patient disappeared from Birmingham and thereafter continued to evade our search. She had to be found, especially since recutting of the block of tissue from the curettings had revealed a tiny area of carcinoma *in situ*, probably of cervical origin. Finally, 21 months after her original positive smear, she was traced. Obvious clinical carcinoma of the portio was found and confirmed by biopsy; the vaginal smear was positive. A Wertheim's hysterectomy was carried out without preliminary radium. Histology showed invasive cancer of the portio with areas of carcinoma *in situ* but the lymph glands were not involved. She has remained well for 18 months.

Comment. Early in the experiment no exact procedure had been laid down. We should have applied our routine investigations for all positive smears, viz., curettage and a ring biopsy of the cervix. Histology would almost certainly have shown carcinoma *in situ* and possibly (but this is conjecture) very early invasive carcinoma.

Although further symptoms might eventually have drawn the patient via her doctor to hospital, there is no way of guessing when her carcinoma might have been diagnosed. Clearly we missed this case as clinicians and credit for alerting the clinical team and insisting on reassessment goes to the cytologist.

Case 2: Typical Carcinoma in situ, *Cervix*

Mrs. G., aged 41, para-2, reported early in the experiment with irregular uterine haemorrhage and occasional post-coital bleeding of 4-months duration. An erosion was present with Nabothian follicles but no biopsy was taken. Uterine curettage and cautery of the cervical erosion was carried out. The endometrial curettings were normal.

The initial pre-operative smear was suspicious (III) but after cautery a further smear from the vagina was taken which proved normal (II). An Ayre's scraping, however, was positive, and the presence of typical carcinoma *in situ* confirmed by subsequent ring biopsy. Since the biopsy in this case amounted to amputation of a large part of the cervix no further treatment was carried out and she has remained well for 4 years.

Case 3: Typical Carcinoma in situ, *Cervix*

Mrs. G., aged 32, para-4, reported a few weeks after the start of this experiment with post-coital bleeding and menorrhagia. She had a large erosion affecting both lips of a split cervix. Our management in the unit for this type of case in 1952 was curettage with often a punch biopsy of the squamo-columnar junction. Cautery of the erosion and careful follow-up in Out-patients completed the case.

A positive smear IV, however, made thorough curettage and a cervical biopsy obligatory but on this occasion, instead of a ring biopsy, a random squamo-columnar biopsy was taken prior to curettage. Typical carcinoma *in situ* was present. A simple total hysterectomy was carried out. Histology showed residual carcinoma *in situ* of the cervix with areas bordering on invasion. The patient has remained well for 4 years.

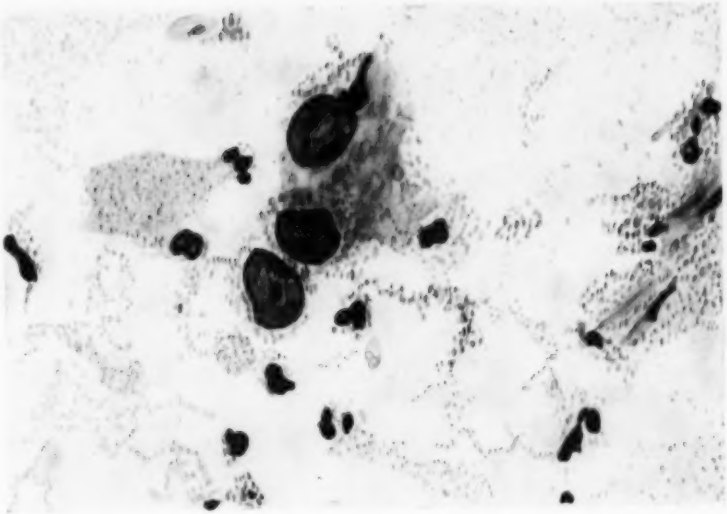

FIG. 1

Case 3. Three malignant nuclei with no cytoplasm (undifferentiated). The chromatin is condensed and outlines the irregular border. Carcinoma *in situ*, typical. ×880.

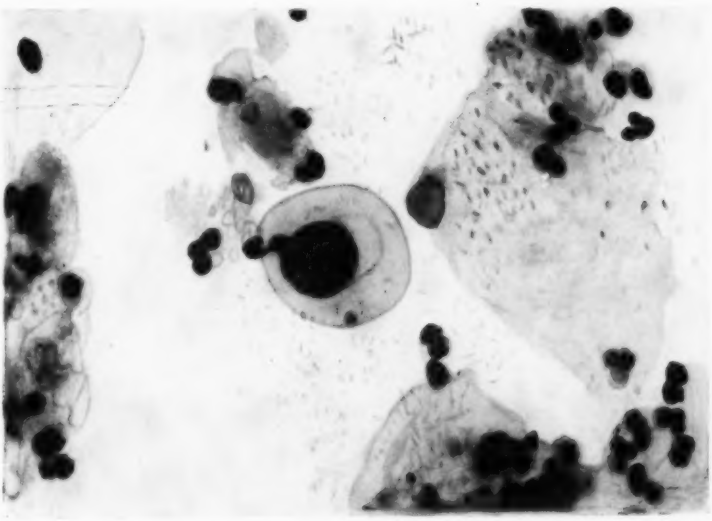

FIG. 2

Case 1. Differentiated malignant squamous cell showing intense condensation of chromatin. This smear was taken 21 months before a final diagnosis of carcinoma of cervix was established. Carcinoma of cervix. ×880.

FIG. 3

Case 6. Three malignant nuclei (Grade IV) on a background of green staining cytoplasm, Döderlein bacilli and polymorphs. Carcinoma *in situ*, equivocal. ×880.

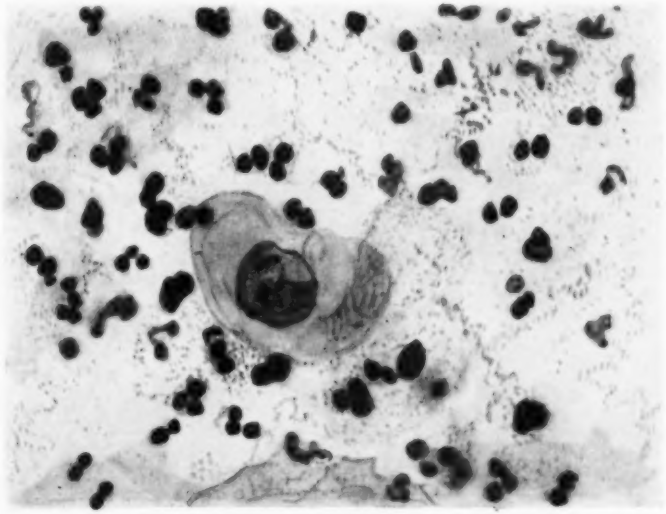

FIG. 4

Case 8. Malignant squamous differentiated cell with "folding" of the nucleus and lobulation. Carcinoma *in situ*, equivocal. ×880.

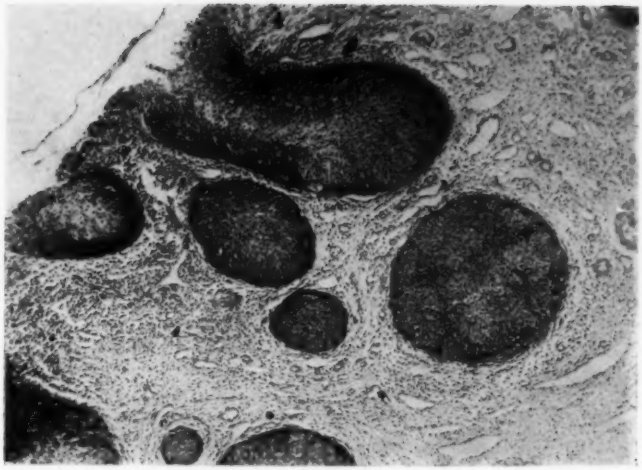

FIG. 5

Case 1. Section of cervix showing carcinoma *in situ* with glandular involvement. ×96.

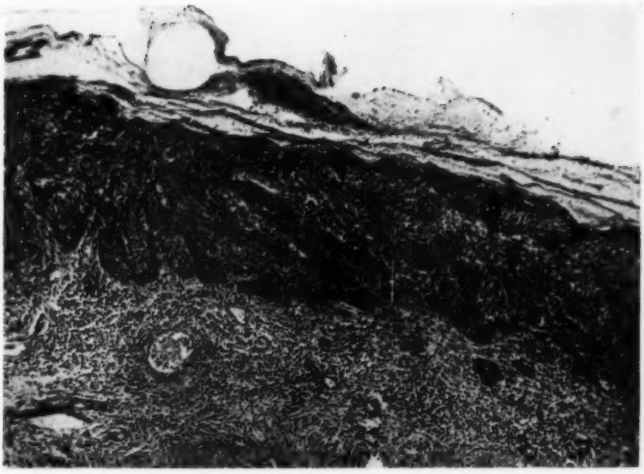

FIG. 6

Case 1. Section of cervix with invasive carcinoma. ×96.

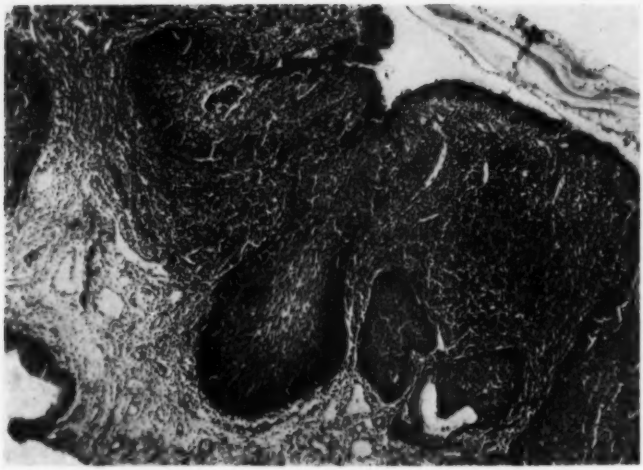

FIG. 7

Case 3. Section of cervix from hysterectomy specimen showing residual carcinoma *in situ* at site of previous biopsy. ×96.

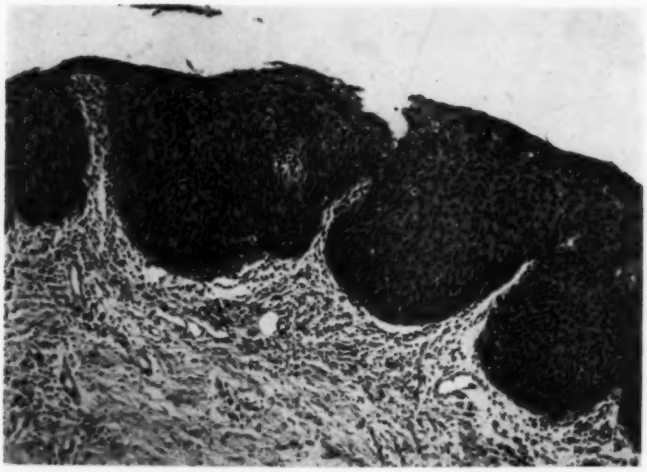

FIG. 8

Case 4. Section of cervix showing typical carcinoma *in situ*; the malignant intra-epithelial cells extend to the free surface. ×96.

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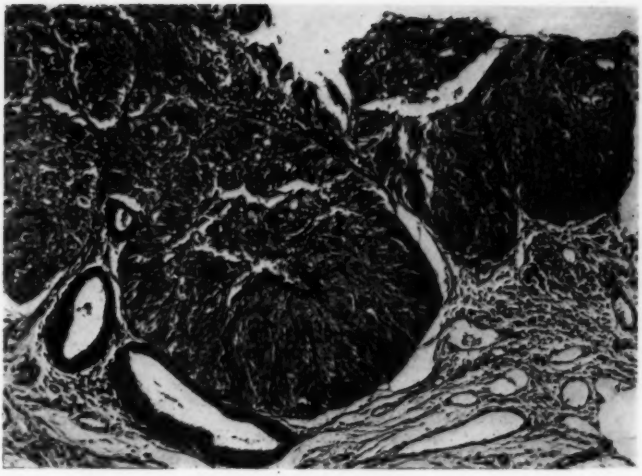

FIG. 9

Case 5. Section of cervix showing typical carcinoma *in situ* with extensive glandular involvement. ×96.

FIG. 10

Section of cervix showing benign epidermization of the mucous glands. This lesion is distinct from equivocal carcinoma *in situ*. ×50.

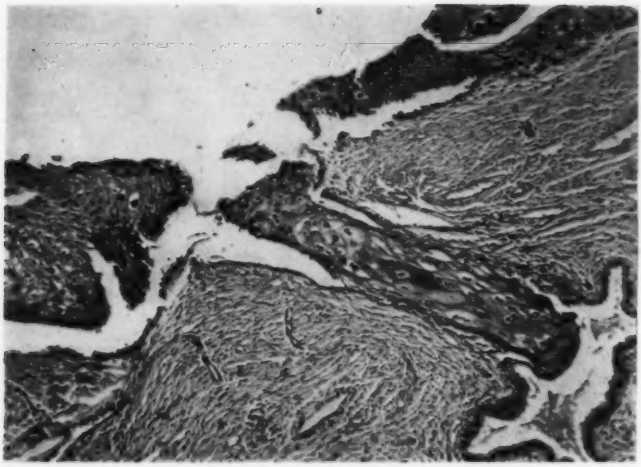

FIG. 11

Case 6. Section of cervix. The surface stratified squamous epithelium contains atypical cells showing mitosis similar to that seen in typical carcinoma *in situ*. These cells, however, do not extend to the free surface of the epithelium. Equivocal carcinoma *in situ*. ×96.

FIG. 12

Case 9. Section of cervix. Intra-epithelial malignant change but with mature or differentiated surface squames. Equivocal carcinoma *in situ*. ×96.

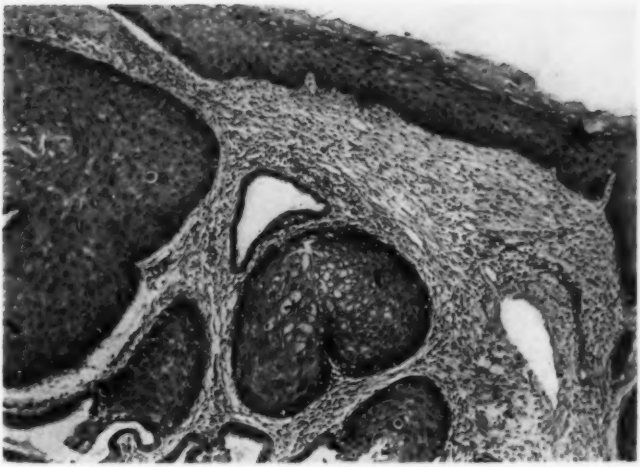

FIG. 13

Case 9. Section of cervix. Equivocal carcinoma *in situ* is involving the mucous glands; atypical mitoses are present in the surface and ectopic squamous epithelium. ×96.

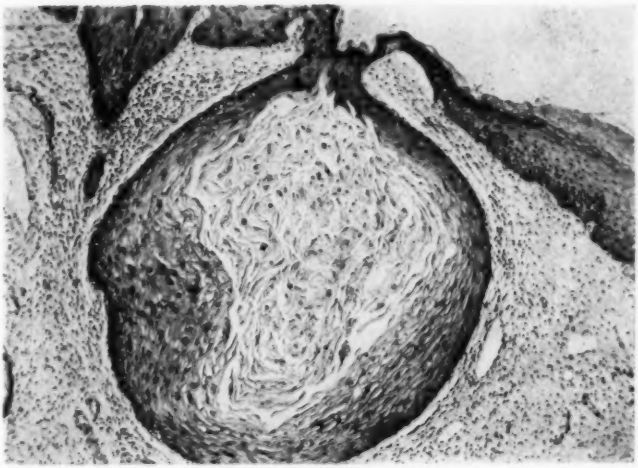

FIG. 14

Case 9. Section of cervix showing cyst-like expansion of the surface epithelium. The abnormal intra-epithelial cells are being desquamated. Vaginal smear positive. ×96.

Case 4: Typical Carcinoma in situ, *Cervix*

Mrs. B., aged 46, para-7, reported early in the experiment with menorrhagia. Gynaecological examination was normal.

A positive smear was ignored in that our routine of dilatation and curettage was carried out without ring biopsy of the cervix. The curettings were normal and the patient was sent home. At follow-up 3 months later a further positive smear compelled us to re-admit the patient. Ring biopsy was carried out and showed typical carcinoma *in situ*. Following this the smears became negative, then after 3 months positive. She was re-admitted and, in view of her age and parity, total hysterectomy was carried out. Residual carcinoma *in situ* was established. The patient has remained well for 4 years.

Case 5: Carcinoma of Vulva Followed by Typical Carcinoma in situ, *Cervix*

Mrs. V., aged 37. This patient had primary amenorrhoea and 2 years previously had required a radical vulvectomy for carcinoma of the vulva. It was then noticed that she had a positive vaginal smear but this was considered to be due to aspiration or contamination of the pipette by cells from the large vulval growth. Following vulvectomy no further smears were taken for 18 months when a positive smear was obtained. Four months later she bled from the vagina. The cervix looked quite normal but with bleeding after amenorrhoea she was admitted. Curettage and a ring biopsy of the cervix were carried out. Typical carcinoma *in situ* of the cervix was found, but certain areas were suspicious of early invasion and a Wertheim's hysterectomy was performed.

Carcinoma *in situ* extended from the squamo-columnar junction along the endocervical canal with involvement of the underlying mucous glands and reached the internal os. A final diagnosis of extensive carcinoma *in situ* without true invasion was made.

Four months after hysterectomy the patient reported with a rapidly growing anal carcinoma. Histologically it appeared to be recurrence from the vulval lesion.

Excision of the rectum and vagina was carried out with terminal colostomy. The patient made a good recovery but, of course, the outlook is very doubtful.

Case 6: Carcinoma in situ (*equivocal*), *Cervix*

Mrs. M., aged 41, para-6, complained of backache, and at examination a slight degree of prolapse with a normal cervix was found. A vaginal smear, however, was positive (IV). Curettage and ring biopsy were carried out. The curettings were normal but the biopsy showed carcinoma *in situ* of equivocal type. She remains well (with negative smears) and is being followed carefully.

Case 7: Carcinoma in situ (*equivocal*), *Cervix*

Mrs. B., aged 46, para-2, complained of severe menorrhagia. She was clinically normal except for a small erosion. The smear was positive, however, and a routine curettage and ring biopsy of the cervix were carried out.

In the cervix there was marked epidermization of the glandular epithelium but in one area there was carcinoma *in situ* of equivocal type. Follow-up over 18 months has been satisfactory, the smears remaining negative.

Case 8: Carcinoma in situ (*equivocal*), *Cervix*

Mrs. D., aged 28, para-3, complained of post-coital bleeding and occasional blood-stained discharge for the previous 4 years which we attributed to a large vascular erosion. No biopsy was taken. The smear, however, although not positive was very suspicious. She was treated by cervical cautery in Out-patients but 2 months later the erosion was still present and bled easily. During a total of 5 months while we observed her in Out-patients the smears varied from suspicious to positive. A ring biopsy showed carcinoma *in situ* of equivocal type. Follow-up over 2 years has been satisfactory. The smears remain negative.

Case 9: Carcinoma in situ (*equivocal*), *Cervix*

Mrs. W., aged 41, para-4, was admitted for curettage on account of menorrhagia. Examination under anaesthesia and curettage were negative but the cytology report was first suspicious then positive. Ring biopsy demonstrated carcinoma *in situ* of equivocal type. She has remained well for 2 years with negative smears.

Case 10: Carcinoma of the Corpus

Mrs. H., aged 62, para-3, was admitted for post-menopausal bleeding. Her first smear was negative; a further smear 2 weeks later was positive (IV). A previous repair coupled with gross obesity made examination difficult even under general anaesthesia, but a vague mass could be felt and was thought to be uterine fibroids. Dilatation of the stenosed cervical remnant was extremely difficult but in view of the positive smear we persisted; finally the uterus was perforated! A week later hysterectomy was decided on but at laparotomy the mass proved to be a simple ovarian cyst which was removed. Hysterectomy was obviously going to be technically very difficult on account of adhesions which completely embedded the uterus in the pelvis. It was considered that carcinoma of the uterus was not proven and the decision made in the theatre was that hysterectomy should not be carried out.

In the early weeks of this experiment we were prepared to watch this patient for a short time at least. Four months after removal of the cyst, positive smears and continued bleeding required re-admission. Dilatation and a most searching curettage, however, again failed to produce any tissue. No ring biopsy of the cervical stump was carried out. A month later with further positive smears she was again admitted with further bleeding. A most difficult total abdominal hysterectomy and right salpingo-oöphorectomy was carried out. On splitting the uterus there was a submucous fibroid in the antero-lateral wall of the uterus. A small adenocarcinoma had been excluded from the exploratory curette by the

fibroid. Histologically the growth was typical adenocarcinoma with solid areas of attempted squamous metaplasia.

Comment. Although without a doubt continued post-menopausal bleeding would have necessitated hysterectomy the positive smears were of value and within our definition of a "pick-up" this case is included.

Ten "Pick-up" Cases

	Complaint	Age	Findings
1	Menorrhagia	34	Carcinoma of cervix.
2	Menorrhagia and post-coital bleeding	41	Carcinoma *in situ*, typical.
3	Menorrhagia	32	Carcinoma *in situ*, typical.
4	Menorrhagia	46	Carcinoma *in situ*, typical.
5	Primary amenorrhoea	37	Carcinoma *in situ*, typical.
6	Slight prolapse	41	Carcinoma *in situ*, equivocal.
7	Menorrhagia	46	Carcinoma *in situ*, equivocal.
8	Bleeding erosion	28	Carcinoma *in situ*, equivocal.
9	Menorrhagia	41	Carcinoma *in situ*, equivocal.
10	Post-menopausal bleeding	62	Carcinoma of the corpus.

Of the 9 lesions of the cervix 6 were reported positive on the 1st smear; 3 were initially only suspicious.

Miscellaneous Findings

(a) *Follow-up Smears*

These were taken from patients already treated by radium or Wertheim's hysterectomy for carcinoma of the cervix or following hysterectomy for carcinoma of the body of the uterus. Eight recurrences gave positive vaginal smears and in 2 of these the positive smears preceded the clinical evidence of recurrence.

(b) *Carcinoma Vulva*

We were surprised to find that 11 out of 13 vaginal smears from proven carcinoma of the vulva were positive, the cells presumably being shed from the vulva into the lower vagina or carried in from the introitus by the aspiration pipette.

(c) *Carcinoma of Ovary*

No malignant cells were obtained on vaginal aspiration in ovarian carcinoma although abdominal aspiration of ascitic fluid from some of these cases produced malignant cells.

(d) *Smear Expediting Admission*

We have not given details of cases where a positive smear expedited the patient's admission. One such example may be given in which a large pessary ulcer started to heal after stilboestrol therapy so that delay and further hormone treatment was planned to ascertain if the ulcer would, in fact, disappear and therefore require no biopsy. The initial smear, however, was positive as were further smears so that outpatient observation and postponement of biopsy was no longer justifiable. Although this type of positive smear was of value to the clinician we have not recorded it as a "pick-up" for the technique of cytology.

(e) *Trichomonas Vaginalis*

Although trichomonas vaginalis is known to be common with and without symptoms of vaginitis it is of interest that in our series of smears trichomonads were seen in 25 per cent of all cases. Trichomonas was present in only one "pick-up" case (Case 1).

Discussion

This report concerns the findings on roughly the first half of our series, viz., 3,337 smears from 2,250 patients.

Cytology in the hands of technicians has proved to be accurate in confirming the presence of carcinoma of the cervix, but in carcinoma of the corpus the method is less accurate. It is noteworthy, however, that invasive carcinoma cervicis has seldom required cytology to lead to a diagnosis, although a confirmatory smear may be of some value to the clinician. The chief value of cytology in our hands is that it has made possible a diagnosis of lesions which may precede invasive carcinoma. Valid comparisons between this and various other studies, unfortunately, cannot be made. For instance, in the series presented by Ayre (1954) and also in that of Nieburgs (1951) cervical scrapings were sometimes taken by general practitioners and sent through the post for examination. In these important studies, therefore, there is no clear definition of the term "pick-up" or surprise positive smear, with the inference that a gynaecologist had examined every case and had failed to diagnose carcinoma; the same can be

said of Anderson's study in Edinburgh (Anderson *et al.*, 1953) where the majority but not all the cases were examined initially by gynaecologists. Similarly, Day of the Strang Prevention Clinic in New York City (1954) states that many of the women attending this so-called "well woman" clinic had signs and symptoms of uterine disease, i.e., once again our definition of a "pick-up" case in gynaecological practice is not applicable. Nevertheless, it is of interest to compare the findings of these workers with our own.

Author	No. of Patients	Carcinoma *in situ*	Invasive Carcinoma
H. E. Nieburgs (U.S.A.)			
(White)	8,112	70 (0·86)	50 (0·6)
(Negro)	2,141	42 (1·9)	60 (2·8)
E. Day, Cancer Detection Clinic (U.S.A.)	16,246	32 (0·2)	4 (0·02)
A. F. Anderson (Edinburgh) ..	3,000	19 (0·6)	8 (0·3)
Professorial Unit (Birmingham) ..	2,250	8 (0·35)	1 (0·05)

Percentages in brackets.

The Economics of Cytology

The cost of finding a single case of carcinoma or carcinoma *in situ* by screening various groups of women with the cytological method has been given as 110 dollars (Ayre, 1954), 500 dollars (Younge, Hertig and Armstrong, 1949) or simply labelled as "prohibitive" (Lombard *et al.*, 1952). We cannot put a figure on our work but simply state that a vast amount of time and a great deal of money has been spent to produce from our Out-patients a total of 2 unsuspected invasive lesions and 8 cases of carcinoma *in situ*.

In our assessment of the cost of a cytological service in the first place we must state that one of us spent 7 months working intensively in cytology in the U.S.A. returning to train our technicians not to be screeners but cytologists able to undertake an increasing volume of work. It takes at least 6 months of intensive training to bring an apt technician up to a reasonable level of competence and perhaps 8 to 10 months before he or she can sign reports. Vaginal smears cannot be read quickly; an average figure of 7 and more often 10 minutes is spent on each slide. Moreover, a cytologist may suffer from eye strain after 4 hours or even less. In our experience, then, after 6 to 8 months a cytologist cannot be expected to read more than 15 to 18 slides each working day.

Furthermore, cytology involves a vast amount of painstaking work not only at the microscope but also in the day to day work within a clinical team. In fact, Novak's calculation (1949) of "some 500 hours of work to reveal one carcinoma" is without a doubt a low estimate.

The Future

Whether or not our colleagues in gynaecology will conclude that a cytological service is a necessity will depend to some extent on how they interpret the value of our 10 cases, a "pick-up" rate of 0·35 per cent. Even if the service is expanded we may expect with the increased number of cases a "pick-up" rate of about the same ratio. With regard to the screening of normal women outside of hospital there are insufficient trained cytologists in this country at present to consider this.

There are, moreover, many difficulties and risks especially in the development of cancerophobia in women submitting themselves repeatedly to vaginal aspiration tests, but the question of our launching into such a study in the future is not closed. (Cancerophobia did not arise in this study since no patient realized that a test was being carried out in any way connected with cancer diagnosis.)

Consider some of the questions which arise when a clinician is presented with a case of carcinoma *in situ*. (*a*) Does carcinoma *in situ* inevitably proceed to the invasive stage; if so, after what number of months or years (Younge, Hertig and Armstrong, 1949; Te Linde, 1953)? (*b*) Does it disappear after pregnancy as suggested by Peckham *et al.* (1954) and Epperson and his colleagues (1951)? (*c*) Does carcinoma *in situ* ever proceed straight to lymphatic involvement?—a question raised by Fletcher (1954). Whatever may be the answers to these

and other questions, the only means of reaching them are by an intensive and prolonged study of the *in situ* lesions of the cervix. We believe, therefore, that cytology should be confined to hospital practice where a close liaison can be maintained with the ordinary clinical and pathological services. Secondly, we believe that an acceptable programme should be drawn up by interested workers for the long term study of the *in situ* lesions.

The question will have to be faced as to whether or not it is ever justified simply to observe a case of carcinoma *in situ*. Te Linde (1953) emphasizes this point and makes it quite clear that his school tended towards a radical view of therapy, i.e., he and his colleagues were prepared to remove carcinoma *in situ* of the cervix on occasions by means of total hysterectomy removing also a parametrial and vaginal cuff. On the other hand, Kottmeier (1951, 1955) takes a much more conservative line in therapy. With our small experience we have been radical; in fact, patients with typical carcinoma *in situ* have been subjected to total hysterectomy (2 cases), high amputation of cervix (1 case), and Wertheim's hysterectomy (1 case). On the other hand, our 4 cases of equivocal carcinoma *in situ* have been subjected to simple ring biopsy. In the Wertheim's hysterectomy there was real anxiety lest there might be co-existing invasive carcinoma as well as carcinoma *in situ*. Until a more complete knowledge of the natural history of carcinoma *in situ* is available no one will really be in a position to gainsay the radical or conservative view. For instance, in younger women desirous of having children local excision of the lesion and careful follow-up may or may not prove to be justified.

Cytology then is one method of revealing carcinoma *in situ* of the cervix. This is its chief function, although very occasionally it may lead to the discovery of invasive carcinoma in gynaecological practice.

We are, therefore, in the position of having a method of discovering a disease, viz., carcinoma *in situ*, without an exact knowledge of its natural history, and, therefore, of its implications for the individual patient. This often leaves doubt as to the proper choice of therapy.

Conclusions

(1) Cytology provides an opportunity to study the natural history of carcinoma *in situ* of the cervix.

(2) Cytology may very occasionally lead to the diagnosis of unsuspected carcinoma of the cervix in gynaecological practice while in confirming the presence of carcinoma of the cervix the method is accurate.

(3) For the future development of the technique a close liaison between the cytologist, pathologist and gynaecologist should be maintained.

Summary

(1) We have attempted to make an exact assay of the value of cytology in the gynaecological service of a Professorial Unit not specially engaged in cancer detection or therapy. The report concerns the first half of our investigations.

(2) The work of cytology has been carried out not by "screeners" but by technicians trained to become responsible for their own reports.

(3) A cytologist (technician) takes at least 6 months to train. Eye fatigue limits microscopy to 3 to 4 hours, or about 16–18 slides per day. A vaginal smear cannot be read accurately in less than 7 minutes per slide; 10 minutes is nearer to the average.

(4) There is also a considerable amount of work apart from microscopy, especially in the teaching of trainees, secretarial and histological work, as well as day to day liaison with the clinicians in the wards and Out-patients.

(5) Errors in cytological interpretation:

(*a*) 11 false positive smears, or 17 per cent of all positive smears, or 0·5 per cent of all smears.

(*b*) 6 false negative smears, or 10 per cent of all malignant cases, 0·26 per cent of all smears.

(6) In the first 2,250 patients examined by the clinicians the following diagnoses were attributable to cytology:

Carcinoma of corpus ..	1
Invasive carcinoma of cervix	1
Carcinoma *in situ*	8

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EXPERIENCE WITH SYNTHETIC OXYTOCIN: THE EFFECTS ON THE CARDIOVASCULAR SYSTEM AND ITS USE FOR THE INDUCTION OF LABOUR AND CONTROL OF THE THIRD STAGE

BY

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THE structure of oxytocin was elucidated, and its chemical synthesis achieved by Du Vigneaud and others (1953). Douglas (1952) stated, "No one has ever injected into a woman via any route, absolutely pure oxytocic . . .". This paper discusses some experience with synthesized oxytocin (Syntocinon or O.T.S. 68, Sandoz), a preparation containing 10 i.u. per ml., 1 i.u. corresponding to 0·02 mg. of synthetic substance.

Before discussing oxytocin, the effects of Pitocin must be briefly referred to so that any differing effects may be noted. Previously most work on the pharmacology and clinical applications of oxytocin has been by the study of Pitocin, a highly purified preparation, but one still containing up to 0·5 units of pressor activity per ml. Now that synthetic oxytocin is available investigation of this substance seemed desirable.

In clinical practice Pitocin has not been used intravenously in biologically large doses either in the first or second stages of labour because of the certainty of uterine tetany and the possibility of uterine rupture, nor has it been used extensively in the management of the third stage because of the possibility of undesirable effects on the cardiovascular system.

These cardiovascular actions have been carefully studied by Woodbury and his colleagues (1940, 1944). There is a marked species difference in responses so that any animal experiments must be accepted with reservation in their application to human physiology. Woodbury noted in males, pregnant and non-pregnant females following an intravenous injection of 3 units of Pitocin, a transient fall in the blood pressure of 30–50 mm. of mercury, returning to normal within 2–3 minutes. This occurred in all cases. He makes it clear that the failure of earlier workers to observe the depressor effect in man can be ascribed to their failure to measure the blood pressure immediately after the injection. Accompanying and following the fall in the blood pressure there was flattening or even disappearance of the T waves in the electrocardiograph. As the T wave changes occurred coincidentally with and not following the fall in the blood pressure Woodbury felt that the changes were not due to diminution in the coronary blood flow following the fall in blood pressure. There was no interference with venous return, no evidence of vasodilatation, nor any change in the heart rate in anaesthetized subjects, and for these reasons it was felt that Pitocin may interfere with the oxidative processes in the heart muscle, causing weak contraction, poor stroke volume and then fall in the blood pressure.

Woodbury concluded that "Oxytocic principle also has cardiovascular actions in man" but carefully added "Of course 'Pitocin' is not a solution of a pure chemical compound. Yet the cardiac effects are associated with the oxytocic fraction of pituitary preparations and may well

be caused by the oxytocic substance or substances."

In the much smaller concentrations used for the pitocin drip Kaufman, Mendelowitz and Ratzan (1953) noted no effect on the blood pressure in 100 cases. Dieckmann *et al.* (1947) described over 1,000 deliveries where pitocin or pituitrin had been given intravenously in a dose of 1 or 2 units to control the third stage, but did not comment on the effects on the blood pressure. In a later paper Dieckmann *et al.* (1950) noted significant hypertension in 11 of 12 patients receiving pituitrin.

Theobald *et al.* (1948) described the use of pituitrin in high dilution as an intravenous drip for the induction of labour. Pitocin has replaced pituitrin for this purpose as it contains less vasopressor material than pituitrin and is now a well accepted aid in the induction of labour.

Pitocin is also used in divided intramuscular injections for the induction of labour, but this method makes no allowance, as does intravenous administration in high dilution, for individual variation in response. Holmes (1954) described uterine responses in different patients varying from nil to tonic contraction with 2 units of pitocin given intramuscularly.

Present Investigation

This paper discusses the effect of synthetic oxytocin on the cardiovascular system of 6 individuals, its use for the induction of labour in 59 cases and for the management of the third stage in 25 cases.

Cardiovascular Actions

This section is in the nature of a preliminary report as further investigation is needed to clarify the mechanisms producing the effects obtained.

Blood Pressure. This was studied in 6 cases. It was originally intended to study the blood pressure response to oxytocin in all patients receiving the drug in the third stage of labour. However it was found in these cases that there were too many uncontrollable factors which might in themselves influence blood pressure, such as the pressor response to effort and varying depths of anaesthesia. Accordingly this study was conducted on 4 volunteer members of the nursing and resident medical staff while conscious, and on 2 anaesthetized patients in the third stage of labour where the depths of anaesthesia were controlled sufficiently well to obtain a constant blood pressure recording before the injection.

In the 6 cases, 2 or more units with a maximum dose of 5 units of oxytocin were given intravenously and the blood pressure recorded every 30 seconds. In all cases there was a significant fall in the blood pressure mainly affecting the diastolic pressure, with a range of fall of 15–40 mm. of mercury. The fall was rapid, occurring within 30 seconds of injection and the return to normal also rapid, always occurring within 3 minutes. There appeared to be a definite relationship between the amount of oxytocin given and the fall in blood pressure, doses of 5 units producing the maximum fall. The response of one subject to an injection of 3 units is shown in Figure 1. In one of the subjects the test was

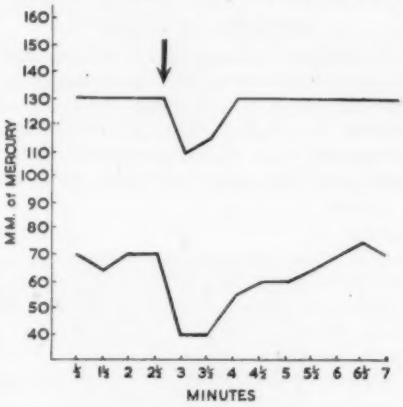

FIG. 1

The effect on blood pressure of 3 units of oxytocin given intravenously. The time of injection is marked by the arrow.

repeated with a continuous tracing of the intra-arterial pressure. The results were similar to those obtained by auscultation, eliminating the risk of observer error.

Electrocardiograph. Significant changes were produced in 3 of the 4 subjects who had tracings taken during the experiment. The subject whose tracing showed no change had an injection of

only 2 units. Three or more units caused flattening or disappearance of the T waves (Fig. 2) and in one apparently healthy male of 28, actual inversion of the T waves. These changes were fully reversed within 3 minutes.

Similar electrocardiographic changes have been recorded by Sjöstrand (1951) during intravenous infusion with adrenalin, so that the possibility that these changes are a reflection of sympathetic response to hypotension cannot be excluded.

Subjective Symptoms. Unpleasant side effects of varying severity were present in the 5 conscious patients. These varied from a mild feeling of fullness in the head with 2 units, to severe abdominal and retrosternal throbbing, frontal headache and a distinct feeling of anxiety with 5 units. In 2 of the subjects the fall in blood pressure was accompanied by hyperventilation. The side effects persisted for up to 6 minutes and were accompanied by marked tachycardia.

Induction of Labour

It is not usual practice in this unit to attempt induction of labour in other than urgent cases unless the cervix is favourable—types 1 and 2 described by Cocks (1955). If the cervix is unfavourable it is digitally stretched daily or second daily, concluding each examination when possible with a limited stripping of membranes. In stubborn cases this is sometimes combined with either an oxytocic drip as described by Mauzy and Donelly (1952) or Carey (1954) or divided intramuscular injections of oxytocin. If the indication for induction is urgent, the membranes are ruptured without regard to the length and dilatation of the cervix.

Twenty-eight patients received oxytocin as a continuous intravenous drip and 31 received intermittent intramuscular injections. The period of gestation of all patients induced is shown in Figure 3.

Intravenous Administration. The technique of intravenous administration was similar to that described for Pitocin by Carey (1954) and Faris and Kahlenberg (1954). Five units of oxytocin were added to 500 ml. of 5 per cent glucose in distilled water, this being connected as a side drip to a further flask of 500 ml. of 5 per cent glucose in distilled water. The rate of flow of the oxytocic solution, initially 10 drops per minute, was increased during a period of ½–1 hour until satisfactory contractions resulted. A Lorand tocograph was used to record uterine contractions. Until the rate of flow was stabilized continuous supervision was carried out by a member of the resident medical staff. There were no cases of tonic contraction of the uterus

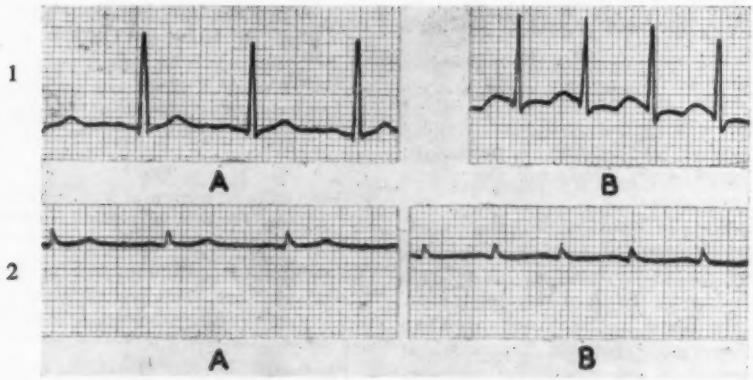

Fig. 2

The effect of intravenous injection of 5 units of oxytocin on the electrocardiograph of 2 individuals. (A) Before injection. (B) After injection.

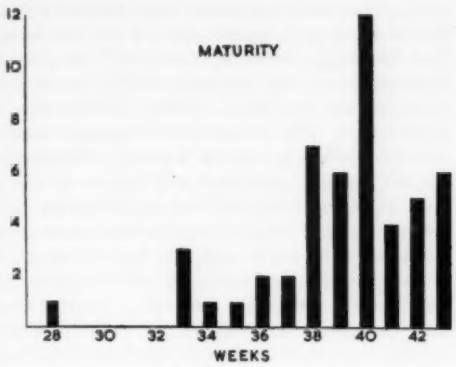

FIG. 3

The maturity of all cases induced.

with this method. Usually rates of flow of less than 35 drops per minute were sufficient (Fig. 4).

FIG. 4

Induction of labour with intravenous oxytocin.

The maximum rate of flow used was 68 drops per minute.

RESULTS

Number of cases treated	28
Indication for induction:	
Toxaemia of pregnancy	18
Accidental haemorrhage	5
Postmaturity	3
Death *in utero*	2
Primigravidae	9
Multigravidae	19
Maternal death	nil
Stillbirths	4
Neonatal deaths	1
Cases in which labour established	27
Failures	1

In all but 8 cases the drip was continued until the time of delivery.

Presentation and Delivery. There were 2 cases of breech presentation and 2 sets of twins. Of the vertex presentations, 20 terminated in spontaneous delivery, 3 in forceps delivery and 1 in Caesarean section. The indication for section was accidental haemorrhage and foetal distress. One patient had previously undergone Caesarean section.

Stillbirths. Of the 4 stillbirths, 3 were macerated, the reason for the induction being foetal death *in utero*, 1 patient, a diabetic, having death *in utero* of twins. The fourth occurred in a postmature primigravida of 19 who was having an oxytocic drip to ripen the cervix. After 6 hours of the infusion and 5½ hours of painless contractions the heart sounds could no longer be heard. The drip was discontinued and labour followed spontaneously 3 days later. This case was the failure listed above as after this the drip was not pursued.

Neonatal Deaths. There was 1 neonatal death occurring in a patient with an accidental haemorrhage requiring interference at 28 weeks. The infant weighed 1 pound 10 ounces and died within 24 hours.

Analysis of Cases. The cases in this group fall into 3 categories:

(1) Those patients who had an oxytocic drip following artificial rupture of membranes. Of the 15 cases in this group, 13 were successfully induced with the first drip. A second drip was required in the remaining 2 cases.

(2) Those patients in whom an oxytocic drip or intermittent intramuscular injections had been used to soften and efface the cervix, followed by artificial rupture of membranes and oxytocic drip. There were 6 cases in this group. Four of these required one course of oxytocin combined with stripping of the membranes to prepare an unfavourable cervix. On the following day the membranes were ruptured and labour induced with an oxytocic drip. One case required 2 successive courses of intramuscular oxytocin to ripen the cervix, labour then being induced by artificial rupture of membranes and oxytocic drip.

(3) Patients who had induction of labour with intravenous oxytocin after artificial rupture of membranes and intramuscular injections had failed to do so. There were 7 cases in this group. Five had one course of intramuscular injections after rupturing the membranes and 2 patients had 2 courses of injections. In all cases labour commenced with the intravenous drip. Clinically this group is important, as failure to induce

labour would mean the prospect of delivery by Caesarean section.

Intramuscular Administration. An initial injection of 1 minim* was given intramuscularly and followed in the absence of contractions by 7 further injections each of 2 minims at half-hourly intervals. There was 1 case of tonic contraction (Fig. 5). When the tonic contraction

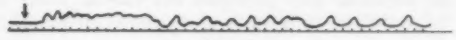

FIG. 5

Tonic contraction following intramuscular injection of 1 minim of oxytocin. Injection given at arrow. Normal labour and delivery followed.

passed off, normal labour and delivery ensued. The usual behaviour was for intermittent contractions to occur after each injection until the course was completed or labour became established (Fig. 6).

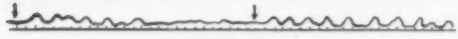

FIG. 6

Induction of labour with intermittent intramuscular injections of oxytocin. One minim given at first arrow, 2 minims at second.

RESULTS

Number of cases treated	31
Indication for induction:	
Toxaemia of pregnancy	24
Postmaturity	5
Accidental haemorrhage	2
Primigravidae	13
Multigravidae	18
Maternal death	1
Stillbirths	1
Neonatal deaths	nil
Cases in which labour induced	23
Cases subsequently induced with intravenous oxytocin	8

Presentation and Delivery. All cases in this group were single pregnancies with the vertex presenting. Of the 23 successfully induced, 5 were delivered with forceps and the remainder spontaneously. There was no Caesarean section.

Maternal Death. There was 1 maternal death in the group. The patient, in the thirty-ninth week of her sixth pregnancy was admitted to the labour ward with an ante-partum haemorrhage. The forewaters were ruptured and 1 minim of oxytocin was given intramuscularly. Moderate contractions developed shortly afterwards; 3 hours later the contractions became much stronger. When the cervix was fully dilated the patient became cyanosed and began to bleed from her mouth, bladder and vagina. A qualitative fibrinogen estimation showed poor clot formation with rapid complete lysis of the clot. A living infant was delivered with forceps and the placenta manually removed. Whole blood and fibrinogen were given, but the patient's condition deteriorated and she died 20 hours after confinement. A clinical diagnosis of amniotic fluid embolism with subsequent hypofibrinogenaemia and fibrinolysis was made. The question would arise as to whether the relationship of the oxytocin to the subsequent strong labour was causal or casual, but as neither pitocin nor oxytocin has been demonstrated to possess an oxytocic effect for more than 40 minutes after intramuscular injection it is a reasonable conclusion that the amniotic embolism was not caused by the oxytocin.

Stillbirths. There was 1 stillbirth. This was a case of accidental haemorrhage in which the foetal heart sounds were absent on admission.

Analysis of Cases. The cases in this group fall into two categories:

(1) Those to whom oxytocin was given intramuscularly after artificial rupture of the membranes. Thirty of the cases were in this group, and of these, 23 were successfully induced. The remaining 7 cases subsequently received intravenous oxytocin.

(2) Cases in which oxytocin was given intramuscularly to ripen the cervix. Only 1 of the cases is in this group and injections were required on two successive days to do so.

Quantity of Oxytocin. This was variable. Four of the cases required as little as 1 minim, 2 cases required 15 minims. The usual quantity necessary was between 3 and 7 minims.

THIRD STAGE

The 25 patients in this group received an intravenous injection of 5 units of oxytocin as the anterior shoulder was born.

* The preparation used in this series contains 10 I.U. per ml. or 15 minims.

Placental expulsion was in general very rapid, 21 of the third stages being completed within 2 minutes. The blood loss was less than 10 fluid ounces in 23 cases, and less than 5 ounces in 20 of these. There were 2 cases of post-partum haemorrhage with blood loss of 23 and 36 fluid ounces. There was 1 manual removal.

It was noticed frequently that uterine relaxation occurred within 20 minutes of the delivery so that supplementary injection of ergometrine was necessary at this time. Both of the patients whose blood loss exceeded 20 fluid ounces were of this type.

All of these patients were anaesthetized. There was no apparent ill effect from oxytocin given in this quantity, but it is not suggested that intravenous oxytocin should become a standard procedure in the management of the third stage. This will be more fully considered in the discussion.

Discussion

The object of this investigation was to study the effects of pure oxytocin and to determine any differences in the behaviour of oxytocin and pitocin.

For convenience the discussion may be divided into 2 sections; the effects of the drug on the foetus, and the effects on the mother.

The Foetus. In this series there were 5 stillbirths. It is emphasized however that 4 of these were macerated, and had been dead when the induction was commenced. In the other case described above where foetal death occurred during a drip designed to soften and efface the cervix, we feel that the foetal death was due to placental insufficiency and that death may have occurred with the onset of normal labour. There was at no time a suggestion of increased uterine tonus, and the contractions were of moderate intensity. It is not now the practice in this unit to administer oxytocics in a postmature pregnancy without first ascertaining the condition of the liquor.

The only risk that the foetus undergoes when an oxytocic is administered is that of interference with the placental blood flow. When oxytocin is administered intravenously with adequate supervision in a dilution of 5 units of 500 ml. this risk is minimal, but it is repeated that supervision must be adequate. When given intramuscularly there is a wide variation in individual response, a disadvantage shared equally by pitocin, so that with this method increased uterine tone or even tonic contraction is a possible development that must be kept constantly in mind. *In hospitals where permanent resident medical staff is available for supervision, intravenous administration is both safer and more likely to induce labour than intramuscular injection.* But it must be remembered that in this country a large number of inductions are carried out in hospitals without resident medical staff and under these circumstances intramuscular administration is safer than unsupervised intravenous drip.

The Mother. The 1 maternal death in this series was due to amniotic fluid embolism and hypofibrinogenaemia, following an ante-partum haemorrhage. The fact that this did not occur until 3 hours after the injection of 1 minim of oxytocin would absolve this from blame as its oxytocic effect would have disappeared more than 2 hours earlier. Neither pitocin nor oxytocin has been demonstrated to possess an oxytocic effect for more than 40 minutes after intramuscular injection.

Oxytocin is an effective aid in the induction of labour. In this series of cases there were no Caesarean sections because of failure to induce labour.

The effects of oxytocin on the cardiovascular system are of great interest. With the doses and concentrations used for the induction of labour no effect either pressor or depressor was noted. With larger doses of 2 or more units intravenously, the preliminary study of these effects confirms Woodbury's statement that "cardiac effects are associated with the oxytocic fraction of pituitary preparation" and are not due to the presence of variable quantities of pressor material in preparations such as pitocin. In all of the cases studied the blood pressure fell significantly and in 3 cases there were significant changes in the electrocardiograph. The changes in the T waves are possibly indicative of some interference with myocardial metabolism. The fact that the T wave actually inverted in 1 case may perhaps be evidence of a temporary coronary insufficiency, or a reflection of sympathetic response to the fall in blood pressure

as described earlier. We feel that at the moment it is unwise to inject more than 2 units of oxytocin intravenously in 1 dose, because of this fall in blood pressure and because the nature of the cardiac and other changes involved in this fall in blood pressure are at present ill understood.

For this reason we feel that oxytocin should not be used intravenously in the management of the third stage even though in our own small series there were no apparent ill effects.

In clinical usage our experience would suggest that for the induction of labour oxytocin (Syntocinon) may be quite safely substituted for pitocin without any more, or less, precautions than are already taken in the use of the latter drug. The effects and results of the two preparations in the induction of labour are indeed indistinguishable.

The cardiovascular effects of oxytocin in a small group of cases, appear to be almost identical with those of pitocin, but the mechanism by which these changes are produced is not clear.

Summary and Conclusions

(1) The use of synthetic oxytocin (Syntocinon or O.T.S. 68 Sandoz) is described.

(2) The technique of the induction of labour both by intravenous and intramuscular injection is described.

(3) The results obtained by both methods are analyzed.

(4) A preliminary report of the effect of oxytocin on the cardiovascular system is incorporated. These effects with doses of 2 or more units intravenously are almost identical with those previously described for pitocin. These effects are a fall in blood pressure and depression or even inversion of the T waves in the electrocardiograph. Unpleasant side effects accompany these changes.

(5) It is concluded that for clinical use the behaviour of synthetic oxytocin is identical to and indistinguishable in its effects from pitocin; that the oxytocin fraction of the pituitary gland has profound, though short-lived, effects on the cardiovascular system when given intravenously in biologically large quantities, and that these effects require further investigation.

Acknowledgments

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CANCER OF THE UTERINE CERVIX: SOME FACTORS INFLUENCING SURVIVAL RATES

BY

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SURVIVAL rates for carcinoma of the cervix are influenced by so many factors other than the method of treatment that it is difficult to determine the efficacy of any new policy or technique. Three points which seem to be of particular importance are: (1) the ratio of the number of cases seeking treatment to the total number of cases occurring in the community at risk; (2) the age composition of the cases reported; and (3) the relative proportion of early to late cases. The purpose of this paper is to discuss these aspects in detail with the aid of statistics drawn from the North-Eastern Region of Scotland.

MATERIAL

Five hundred and fifty-two cases of carcinoma of the cervix were seen during the 12 years 1942–1953 in the Gynaecological and Radiotherapy Departments of Aberdeen Royal Infirmary. Where histological examination was not performed, the clinical features were so characteristic as to leave no doubt as to the diagnosis. A few cases have been rejected where the exact site of origin of the neoplasm was uncertain. Cases not treated or treated by radium in private nursing homes or other institutions are included. Some women for whom no records can be traced may have been operated upon by general surgeons but the numbers are undoubtedly so few as to have no effect on the conclusions. An attempt has been made to compute the number of cases not referred for specialist advice.

INCIDENCE

Of the 552 patients, 255 lived in Aberdeen City and 297 in the remainder of the North-Eastern Region. The average number of new cases from the City each year was 21 and as this figure varied very little year by year it seems likely that practically every woman in the City with cancer of the cervix is seen by a gynaecologist. The total population of the Region is about 500,000, divided between the City and the rural areas in the proportion of 3 to 5. Assuming that the incidence of cervical cancer is similar in town and country, the latter should provide some 35 cases per year as against the former's 21. For the Region as a whole the annual number of cases should be between 55 and 60, giving a total of 650 to 720 in 12 years. The actual number was only 552 so that possibly only about 75 per cent of all cases were referred to hospital. Since the "missing" cases may have had more advanced lesions than the others (the practi-

TABLE I

Age Distribution of Complete Series

Age in years ..	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84
Total: 552 ..	1	10	26	52	69	81	73	84	66	47	26	11	6
Per cent distribution ..	0·2	1·8	4·7	9·4	12·5	14·7	13·2	15·2	12·0	8·5	4·7	2·0	1·1
		16·1				67·6					16·3		

tioners considering it not worthwhile referring them to hospital), their absence may have exerted a beneficial effect on the survival rates. For this reason it would be preferable to study the City cases only but because of the small numbers involved it has been necessary for some purposes to deal with the series as a whole.

Age Composition

The age distribution of the complete series, as shown in Table I, is symmetrically arranged around a mean of 52·7 years. Within the wide range of 20 to 84 years, 67·6 per cent (about two-thirds) of the patients were aged 40 to 64 years, 16·1 per cent (one-sixth) under 40 years, and 16·3 per cent (one-sixth) 65 years and over. The City cases show an almost identical age pattern.

Clinical Stage Classification

Table II shows the distribution by clinical stages of the 253 cases in 1942–1947, and the 299 cases in 1948–1953. During the second 6-year period there has been a 5 per cent increase in the proportion of cases assigned to Stages I and II, 66·0 per cent as against 60·9 per cent. This change affects Stage I in particular, the actual numbers increasing from 42 to 86, and the proportion from 16·6 to 29·0 per cent. It is important to determine whether this reflects a true increase in the proportion of more favourable cases or an alteration in the criteria used in assessing the extent of the lesion. This question has been examined with reference to age and to duration of symptoms, both of which are correlated with clinical stage.

Table II
Clinical Stage Distribution

Clinical Stage	1942–1947		1948–1953	
	No.	Per cent	No.	Per cent
I	42	16·6	86	29·0
II	112	44·3	111	37·0
III	71	28·0	78	26·0
IV	28	11·1	24	8·0
Total ..	253		299	

For the series as a whole, the average age of Stage I cases is 50·5 years, Stage II—52·5 years, Stage III—53·0 years, and Stage IV—57·6 years. Thus the stage distribution of any series will be related in some measure to its age composition. The more favourable stage distribution of the 1948–1953 group of cases is not, however, due to a younger average age for in fact rather more women were aged 65 years and over than during 1942–1947.

For the complete series, the average time between the onset of symptoms and the diagnosis of cancer was 6 months, ranging from just over 5 months for Stage I to nearly 10 months for Stage IV cases. During 1942–1947, 34·0 per cent of all patients reported within 3 months of the appearance of irregular bleeding; in 1948–1953, this figure rose to 42·5 per cent. It is possible, therefore, that the increased proportion of cases in the earlier stages represents a real increase in more favourable cases.

Results of Treatment

Throughout the 12-year period, the standard method of treatment was the application of radium; 50 mg. into the uterus and 37·5 mg. into each lateral vaginal fornix for 24 hours, 3 treatments being given at intervals of 1 and 2 weeks. External radiation therapy was rarely given. Surgery was not employed during the earlier years. During the period 1948–1953, 67 out of 299 patients (about 2 out of 9) were operated upon: 1 in 3 Stage I cases, 1 in 4 Stage II, 1 in 9 Stage III, and 1 in 12 Stage IV. As regards age, surgery was carried out on 1 patient in 2 under 40 years, 1 in 5 in the age-group 40–64 years, and only once among 50 patients aged 65 years and over. The types of operation were as follows: pelvic exenteration—4; Wertheim hysterectomy and lymphadenectomy after radium—45; lymphadenectomy after radium—12; Wertheim hysterectomy and lymphadenectomy without previous radium—6. None of the patients received either pre- or post-operative X-ray therapy. As the figures show, localized lesions and youth constituted the main indications for surgery, but general fitness and degree of obesity were also taken into account. No attempt was made to select cases on histological or cytological grounds, and operation was per-

formed in those cases who had had radium before the clinical response to radiation could be judged.

Table III presents the 5-year survival rate for all cases seen in 1942–1947, together with the rates for the individual stages. For all cases seen the survival rate is 26·9 per cent, for all cases treated 28·3 per cent; the 13 cases not treated were all in Stage IV. Table IV shows the survival rates for patients aged under and over 50 years; the results for the individual stages are not dissimilar, and the poorer overall survival rate for the older group would appear to be due to the facts that 45 per cent of them had lesions in Stages III and IV as against only 30 per cent of the younger group, and that 67·7 per cent of all Stage III and IV cases were over 50 years of age.

TABLE III
Survival at 5 Years for All Cases, 1942–1947
(Percentage figures in parenthesis)

Clinical Stage	Total	Died Within 5 Years	Outcome Unknown	Alive at 5 Years+
I	42	15	4	23 (54·8)
II	112	74	5	33 (29·5)
III	71	57	2	12 (16·9)
IV	28	28	0	0 (nil)
Total ..	253	174	11	68 (26·9)
Treated cases	240	161	11	68 (28·3)

N.B.—13 untreated cases all in Stage IV.

With regard to the later years, only an interim report can be given. During the period 1948–1951, 198 cases were seen and 35 of these were operated upon. The survival rate to mid-1955 was 41·9 per cent (83 out of 198) and the ultimate 5-year survival figure will probably not differ greatly from that applicable to 1942–1947. Of 30 Stage I and II cases operated upon during 1948–1951, 19 were alive at mid-1955—an interim survival rate of 63·3 per cent; of 102 Stage I and II cases treated by radiotherapy during the same period, 51 survived or 50 per cent. If women aged 65 years and over are omitted from the radiotherapy group—since no woman of this age was operated upon during the years in question—the survival rate for the remainder is 52·6 per cent (41 out of 78). The difference of some 10 per cent is, however, less striking than might at first appear when one considers that only fit women were submitted to surgery and that all late Stage II cases were treated by radiotherapy alone.

Between 1948 and 1953, 56 cases in Stages I and II were submitted to lymphadenectomy, with or without radical hysterectomy; involved nodes were found on microscopic examination of material removed from 16 of these cases. Of the 16 women with positive nodes, 8 were alive at mid-1955. Of the 40 patients with negative nodes, 36 survived at mid-1955, but there is no reason to suppose that the outlook for these cases was improved by operation. It would thus appear that, although 56 women were submitted to surgery, only 8 at most derived any benefit from operation. Two of these women have now survived 5 years from the time of operation, 4 have lived between 3 and 4 years, and 2 between 2 and 3 years. Although no patient died as the result of opera-

TABLE IV
Survival at 5 Years for All Cases, 1942–1947
(According to age and clinical stage)

Clinical Stage	Age in Years					
	Under 50 Years			50 Years and Over		
	Total	Survivors	Per cent	Total	Survivors	Per cent
I	21	12	57·1	21	11	52·4
II	53	15	28·3	59	18	30·5
III	26	4	15·4	45	8	17·8
IV	6	0	Nil	22	0	Nil
Total (253)	106	31	29·2	147	37	25·2

tion, some developed serious complications. In one case, where it was necessary to ligate the external iliac artery, gangrene of the foot ensued and amputation was required; the patient died of cancer 18 months later. Two women developed a uretero-vaginal fistula, one being treated by nephrectomy and the other by transplantation of the ureter into the bladder. One woman sustained a vesico-vaginal fistula which closed spontaneously. It is probable that the operative mortality in a large series might be about 1 per cent, and the incidence of serious complications in the region of 5 per cent, figures which are in agreement with those of Meigs (1954).

Discussion

Survival statistics from individual hospitals are of limited value. In large populations the institution to which a particular case is referred is probably a matter of chance. Even when a hospital claims to deal with all cases from a given district, the figures must be accepted with caution. Southampton alone of all British centres contributing to the International Reports is said to see all cases occurring in a well-defined geographical area; nevertheless, although in the 10 years ending 1942 38 new cases were seen on the average each year, this figure rose to 64 between 1943 and 1947, and to 76 in 1947—exactly double the average for the earlier years. It would be dangerous to judge the standard of treatment over the years by the survival rates without taking into account the great increase in the annual number of cases. The other British centres which publish reports do not claim that their cases are unselected but here again the annual numbers have been steadily increasing. If the explanation be that elderly women or those with advanced lesions were less frequently referred to hospital in the past, their appearance in recent years would obscure any effect of improved methods of treatment. The falling death rate from cancer of the uterus shown in the Registrar-General's Reports may be due more to the fact that many more cases are nowadays receiving treatment than to better methods of treatment.

Calculations based on Aberdeen City experience—an average of 21 new cases of cervical cancer per annum in a population of 185,232—suggest that the annual incidence of new cases of the disease may be in the region of 115 per 1,000,000 total population. This agrees with Maliphant's estimate (1949) that he would expect 28 to 30 cases to present annually in Cardiff, population about 250,000, an incidence of 112 to 120 per 1,000,000. Since the disease is very rare under the age of 20 years, it is more reasonable to state the incidence in relation to the number of women at risk after that age; the figure for Aberdeen City is 30 per 100,000 female population aged 20 years and over. If reference is made only to married, including widowed and divorced, women aged 20 years and over, the incidence is 40 per 100,000 such women per year. These three estimates of incidence provide useful indices by which to measure past and present experience in any one region and also serve to indicate the comparability of clinical series derived from different sources. The incidence need not, of course, be the same in different areas because of differences in age composition and social structure of the population. Stocks (1955) reports that the death rate from cervical cancer shows a relationship with overcrowding, social class distribution and the predominant industry of the area, the highest death rates being found in textile towns and seaports.

The age pattern of any reported series should also be considered. Table V gives some information about the age composition of 4 groups of cases. While the Boston (Morris and Meigs, 1950) and Aberdeen data are similar, the Cardiff material (Maliphant, 1949) is deficient in elderly women and the New York series (Speert, 1948) includes a surprising number of women aged under 40 years. Whatever the explanation of these differences, it is obvious that they must influence survival rates. Deaths from intercurrent disease are more frequent in older women, and in Aberdeen at least elderly women tend to delay longer than younger patients in seeking advice and the lesions are more often in an advanced stage.

The allocation of cases to clinical stages according to the estimated local extent of the tumour is intended to provide reliable data both for prognostic and comparative purposes but

TABLE V

Age Distribution of 4 Series of Cervical Cancer Cases

Centre	No. of Cases	Average Age (years)	Percentage Distribution (by age)		
			20–39	40–64	65–
Aberdeen	552	52·7	16·1	67·6	16·3
Cardiff	1,200	51·0	16·2	74·3	9·7
Boston	1,938	51·0	16·9	69·5	13·3
New York	622	47·3	26·9	67·0	4·9

experience shows that even in the hands of experts staging is inaccurate. In Great Britain the proportion of cases in Stage I ranges from 7·1 per cent in Manchester to 22·6 per cent in University College Hospital, London, and in Stage IV from 0·9 per cent in Cardiff to 14·9 per cent in Northwood, London (Heyman *et al.*, 1954). There would appear to be two explanations for these gross variations: that the total material is unrepresentative and that the standards of classification vary. Since Southampton's figures are said to be regional, they can be compared with those from Aberdeen. During 1943–1947, 303 cases were treated in Southampton with a 5-year survival figure of 33·3 per cent; the cases were distributed as follows: Stage I—7·9 per cent, Stage II—38·6 per cent, Stage III—44·2 per cent, and Stage IV—9·3 per cent. In Aberdeen during 1942–1947, 240 cases were treated with a 5-year survival rate of 28·3 per cent, the distribution being: Stage I—17·5 per cent, Stage II—46·7 per cent, Stage III—29·6 per cent, and Stage IV—6·2 per cent. The Southampton percentage for Stages I and II combined is 46·5, whereas for Aberdeen this figure is 64·2. More efficient methods of treatment in Southampton might give a survival rate which is 5 per cent better than in Aberdeen, but this would be unlikely if the Southampton series were so weighted with advanced cases as the figures suggest.

Even within one unit staging of cervical carcinoma by clinical examination has proved unreliable. Philip (1949) reports that in Aberdeen during 1930–1936, 71 Stage I cases were treated with a 5-year survival rate of 53 per cent, and 67 Stage II cases with a survival rate of 18 per cent; for the 138 cases in Stages I and II combined, the survival figure is 36·2 per cent. During 1942–1947, 42 Stage I cases were treated with a survival rate of 54·8 per cent, and 112 Stage II cases with a survival rate of 29·5 per cent; for the 154 cases in Stages I and II combined, the 5-year survival rate is 36·4 per cent, virtually identical with that for the earlier period despite the fact that the proportion of cases allotted to Stage II was much higher in 1942–1947. Obviously some change must have occurred in the standards of classification after 1936 but since the survival rate for Stage I was almost the same in both periods, it appears that the policy of assigning a high proportion of cases to Stage I during 1930–1936 was justified. If the 154 cases of 1942–1947 had been classified in the same way as in 1930–1936, 75 would have been placed in Stage I (instead of only 42) and to these a survival rate of 53 to 55 per cent would have been applicable; for the other 79 cases, of course, the survival rate would have been only about 18 per cent. The overall survival rate would have remained unchanged at about 36 per cent, but one would have had a much more refined index of prognosis. Since the method of treatment was the same during both periods, these points may be somewhat academic; but if, for instance, a different technique of treating Stage II lesions had been employed during the later years one might erroneously have concluded that its effect had been to raise the survival rate for such cases from 18 to 29·5 per cent.

These variations in the classification of cervical carcinoma will make it difficult to measure the effect of surgery as practised in Aberdeen during the years 1948–1953. Judged by the duration of symptoms, the 1948–1953 cases seem on the whole to be more favourable

than those in the years 1942–1947, and better results should be obtained even if surgery has not contributed any benefit.

The present method of classification has two main weaknesses: (1) the interpretation of the findings is subject to individual judgment; (2) Stage II by definition includes a very wide range of cases differing greatly in their likely response to treatment. Where the cervix is short or the demarcation between cervix and vagina indistinct, opinion may differ as to whether a lesion should be placed in Stage I or Stage II; again, parametrial thickening may be inflammatory or neoplastic in nature, and it may be difficult to decide whether to allot the case to Stage II or Stage III. Although Heyman *et al.* (1955) provide full instructions on these points, the published data show that not even the most carefully framed rules can be uniformly interpreted.

Morris and Meigs (1950) suggest that Stage II might with profit be subdivided but one is inclined to agree with Heyman (1950) that this would increase rather than decrease confusion. A more satisfactory step might be to eliminate altogether the present Stage II. Both proposals are, however, hampered by the absence of any convenient anatomical point of reference between the outer aspect of the cervix and the lateral pelvic wall. There might nevertheless be something to be said for a purely subjective system of classification into three groups: early, intermediate and late. The first would include all lesions presently placed in Stage I together with those Stage II lesions showing only limited extension beyond the cervix. By and large cases allotted to this group could be regarded as technically operable, whether or not a surgical policy were in fact pursued. It would thus become possible to compare surgical results with those obtained by radiotherapy in an equivalent series of cases; of course, other factors such as age and medical fitness also govern the decision to operate and these, together with the malignancy of the tumour, no doubt affect the outcome just as much as does the extent of the disease at the time of treatment. The late group would include all cases which experience has shown to be unlikely to survive for 5 years no matter what form of treatment is given—the present Stage IV cases and those extensive Stage III lesions where it is impossible adequately to irradiate the whole of the involved area. There would naturally be a tendency to place a majority of cases in the intermediate group, just as there is at present a trend to classify a large number of cases as Stage II. This is not, however, a serious disadvantage as the prognosis for most cases of cervical cancer is very doubtful.

Because of the various factors which have been discussed, it is difficult to ascertain whether surgery as practised in Aberdeen has had any beneficial effect, but one is probably justified in concluding that the place for operation is limited. All the published evidence suggests that only about 1 patient in 5 with positive nodes survives for 5 years after operation, and it is likely that modern irradiation methods can achieve a similar effect. Recently claims have been made that it may be possible to differentiate by histology and cytology those tumours which are radiocurable from those which are not but there is no means of determining whether surgical removal would have been successful in those cases where irradiation alone has failed. The effect of surgery can be judged only by statistical analysis and, as has been shown, this is by no means a simple matter.

Personal experience suggests that at most no more than 2 cases out of 5 in any really representative series are likely to be technically operable. Surgery on advanced cases is both difficult and dangerous, and there is no evidence that it can produce better results than radiotherapy. But even if from the viewpoint of local extent of the carcinoma surgical removal is feasible, one must also consider whether or not the patient is a suitable candidate for major surgery. If the elderly, the grossly obese and the medically unfit are excluded, it is probable that only upon perhaps 1 patient in 5 can operation justifiably be performed. It is, of course, well known that Bonney (1941) reported an operability rate of over 60 per cent, but this figure was based on a limited sample of his total material and it is likely that his cases were to some extent selected before he saw them; moreover, during most of the period concerned radiotherapy was in its infancy. If operation is

practicable in only one-fifth of an unselected series, then the few cases operated upon would have to show substantially better results than radiotherapy in order to exert any beneficial influence on the overall survival rates.

Advances in irradiation techniques offer the best hope of improvement since the benefits can be applied to the majority of cases, but even when the point at issue is the relative advantage of one irradiation procedure over another full account must still be taken of the many factors other than the actual method of treatment which exert such an important influence on survival rates.

Summary

Survival rates for cancer of the cervix are influenced by many factors other than the method of treatment. The problem is illustrated by experience in the North-Eastern Region of Scotland.

Reports from individual centres are of limited value because the material is unlikely to be representative. Regional data are more reliable but some indication must be given of what proportion of all cases occurring in the area is included in the series. Published reports show that the annual number of cases seeking treatment is steadily increasing. The falling death rate from cancer of the uterus shown in the Registrar-General's Reports may be due more to the fact that many more cases are receiving treatment than to improved methods of treatment.

The age composition of the cases is important since, apart from more deaths from intercurrent disease, survival rates for older women are adversely affected by their greater tendency to delay seeking advice.

The standard classification of cases according to the local extent of the lesion fails to provide sufficiently reliable information for prognostic and comparative purposes. It is suggested that Stage II might be eliminated and the cases placed in three groups—early, intermediate and late. The first would include all technically operable cases (whether or not clinically operable), thus providing a basis for direct comparison between surgery and radiotherapy, at least in so far as local spread of the tumour governs the outcome.

There is no convincing evidence that surgery applied empirically can achieve better results than radiotherapy in equivalent cases. Operation is probably practicable in at most 1 case out of 5 in any unselected series; to exert any significant influence on overall survival rates, the 20 per cent of cases operated upon would have to show substantially better results than similar cases treated by irradiation.

Since radiotherapy can be applied to a high proportion of cases, advances in irradiation techniques offer the best hope of improvement. When comparing one irradiation procedure with another, one must, however, also take into account the various statistical factors which have been discussed.

Appreciation is expressed to Professor Dugald Baird for his advice in the preparation of this paper.

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CONGENITAL TOXOPLASMOSIS SIMULATING HAEMOLYTIC DISEASE OF THE NEWBORN

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FOETAL hydrops suggests haemolytic disease of the newborn. There are, however, other, less common, causes, among these toxoplasmosis.

The purpose of this paper is to report three cases of congenital toxoplasmosis which at first gave rise to suspicions of haemolytic disease.

Case 1. Baby D. was born on 8th July, 1954.

Abnormalities noted during this, the mother's first pregnancy, were: excessive gain in weight, hydramnios, frequency of micturition and profuse vaginal discharge. Labour lasted 16 hours. Foetal heart sounds ceased 10 minutes before delivery.

The baby was stillborn, severely hydropic and weighed 4 pounds 13¾ ounces. The placenta was unduly large, fleshy pink in colour, friable and oedematous.

POST-MORTEM EXAMINATION

When the skull was opened numerous small whitish-yellow, necrotic areas were seen beneath the pia-arachnoid on the surfaces of both cerebral hemispheres. During the removal of the brain yellowish fluid escaped in quantity suggesting hydrocephalus. Multiple soft, yellowish, necrotic areas were found throughout both cerebral hemispheres, particularly around the lateral ventricles. The hind brain showed no apparent lesion, but its softness precluded detailed examination.

The serous sacs contained much fluid. Nothing of note was found in the heart and lungs.

The liver and spleen were enlarged, the latter being 4 times the usual size.

The kidneys and suprarenals did not seem unusual.

HISTOLOGY

Brain. Sections showed multiple areas of necrosis and calcification. These were particularly abundant in the superficial cortical zone, and in the subependymal region. The areas of calcium deposition were generally surrounded by an intense inflammatory reaction, predominantly histiocytic, but with varying numbers of plasma cells, lymphocytes and polymorphonuclear leucocytes. Some of the blood vessels in relation to necrotic foci were involved in the inflammatory reaction. The choroid plexus was heavily infiltrated with acute and chronic inflammatory cells.

Typical toxoplasma pseudocysts were found, not in the necrotic areas, but in the adjacent apparently healthy tissue, 1–2 mm. away (Fig. 1). Among the necrotic debris were aggregations of granular material which had some resemblance to both pseudocysts and terminal colonies, but had no surrounding membrane (Figs. 2 and 3).

Heart. The subepicardial region and, to a

lesser extent, the myocardium were infiltrated by lymphocytes, histiocytes and plasma cells. No necrosis of the muscle fibres was present. No toxoplasma could be found.

Liver. Haemopoiesis was excessive, even allowing for prematurity. Much of it was of primitive type. The Prussian blue reaction was negative.

Spleen. There was an excess of erythropoietic cells. The Prussian blue reaction was negative.

Kidney. A narrow neogenic zone remained, indicative of prematurity. As in the liver, haemopoiesis was excessive even allowing for the prematurity (Fig. 4). Many of the red cells in the renal vessels were of primitive type (Fig. 5).

Eye. Posterior uveitis was present. There was no evidence of involvement of the optic nerve. Aggregations of bodies resembling toxoplasms were found in the disorganized retina.

Pancreas and Suprarenal. Nothing unusual.

Placenta. The villi were swollen and oedematous, as in haemolytic disease.

Serology

Blood Grouping

Mother: Group A Rh. positive.

Mother's serum and baby's cells: Indirect Coombs's test negative. No abnormal antibodies found.

Father: Group B Rh. negative.

Baby: Group A Rh. positive. Direct Coombs's test negative.

Wassermann: Mother—negative.

Toxoplasma Antibodies

	Dye Test	C.F.T.
Baby:		
12th July, 1954		
Cord Blood	1/2,500	1/32
Heart Blood	1/5,750	1/32
Mother:		
12th July, 1954	1/12,500	1/32
27th July, 1954	1/18,000	1/640
25th January, 1955	1/7,000	1/64
21st March, 1955	1/2,000	1/16
21st April, 1955	1/220	1/32
19th May, 1955	1/275	1/64
17th June, 1955	1/240	1/64
18th July, 1955	1/65	1/64
28th July, 1955	1/57	1/64
Mother (*continued*):		
8th August, 1955	1/800	
11th August, 1955	1/1,500	1/64
After birth of succeeding child:		
31st August, 1955	1/1,000	1/32
Succeeding healthy baby:		
31st August, 1955	1/1,250	1/64
Father:		
22nd July, 1954	1/4	1/4

Isolation of Toxoplasma

At first it was thought that attempts to isolate the parasite would fail. A suspension of the brain was inoculated on 8th July, 1954 in Edinburgh into two guinea pigs intraperitoneally, two mice by the same route, and two mice intracerebrally. One of the guinea pigs was killed on 16th July, 1954, but no toxoplasms were found in smears of peritoneum, spleen, liver or brain. None the less a suspension of these tissues was inoculated into the peritoneal cavity of two guinea pigs and two mice.

Apart from one passage mouse which died of ante-partum haemorrhage nineteen days after inoculation, and the guinea pig which was killed, all the original and passage animals were still alive on 17th September, 1954. On that date one of the original mice and the surviving passage mouse were killed in Sheffield. No toxoplasms were found, but a suspension of their brains, livers, and spleens was inoculated intracerebrally and intraperitoneally into two mice. In ten days these looked ill, were killed and toxoplasms were found in their peritoneal fluids.

The rest of the original mice were killed on 27th September, 1954. Again no toxoplasms were found but combined intracerebral and intraperitoneal inoculation of a suspension of their organs into further mice produced toxoplasmosis.

Following on this success blood was taken from the remaining original and the two passage guinea pigs which had been kept in Edinburgh. High titre dye test results were obtained on their sera.

The original guinea pig was killed on the 95th day (18th October, 1954). No toxoplasms were found in it, nor did inoculation of mice with its peritoneal exudate, spleen and liver (brain was not included) produce toxoplasmosis even after four blind passages.

One of the passage guinea pigs was killed on the 74th day (28th September, 1954) after inoculation. No toxoplasms were found in it, nor did combined intracerebral and intraperitoneal inoculation of a suspension of its spleen and liver (brain was not included) produce toxoplasmosis in mice even after three blind passages. The other passage guinea pig was killed on the 250th day (18th March, 1955) and toxoplasms were isolated in the first set of mice inoculated intraperitoneally and intracerebrally with brain suspension.

This guinea pig was a virgin female at the time of inoculation on 16th July, 1954. She was caged with a boar for the last two weeks of October, 1954, and gave birth to two healthy females on 9th January, 1955.

Case 2. Baby T. was born on 6th December, 1954.

The mother had been subject to epileptic fits, but the last was 8 years before this pregnancy, during which she was well.

The membranes ruptured prematurely and she was admitted to hospital in labour at thirty-five and a half weeks. Labour lasted 11 hours. Presentation was breech and forceps were applied to the aftercoming head.

In spite of endotracheal oxygen, the baby gasped only a few times and died.

Apart from emphysematous swelling of the neck, no external abnormalities were noted; in particular there was no external evidence of hydrocephalus nor of oedema. The placenta was large and flabby, as in haemolytic disease.

Post-mortem Examination

Brain. When the skull was opened deep yellow fluid escaped, probably from the lateral ventricles. There was considerable subdural haemorrhage with large amounts of blood clot lying on the superior surface of each half of the tentorium cerebelli and extending around the mid-brain. The pia-arachnoid was healthy and no necrosis or calcification was obvious on the surface of the brain. Section, however, showed numerous areas of necrosis and calcification, most pronounced in the walls of the greatly dilated ventricles.

Thorax. Bilateral pneumothorax was present, the lungs lying far back in the pleural cavities. The pericardium was healthy and the heart was of appropriate size and developmentally normal.

Abdomen. Both liver and spleen were enlarged, the spleen being approximately three times the usual size. The Prussian blue reaction on both organs was negative. Kidneys and suprarenals showed no pathological change.

Eyes. After fixation the eyes showed on section a small whitish, opaque lesion on the surface of the retina immediately posterior to the ciliary body.

Histology

The histological features were almost the same as in Case 1. The cerebral lesions were similar. Toxoplasma pseudocysts (Fig. 6), terminal colonies (Fig. 7) and aggregations of granular material (Fig. 8), similar to those in Case 1, were found. Microscopy showed chorio-retinitis and myocarditis. The liver and spleen both showed excessive haemopoiesis much of this, in the liver, being of primitive type.

Serology

Blood Grouping

Mother: Group O Rh. positive. No abnormal antibodies found.

Baby: Coombs's test negative.

A subsequent healthy baby was born in February, 1956.

Toxoplasma Antibodies

	Dye Test	C.F.T.
Baby:		
9th December, 1954	1/1,300	1/240
Mother:		
16th December, 1954	1/1,050	1/64
14th November, 1955	1/280	1/20
19th January, 1956	1/54	1/20
Father:		
19th May, 1955	1/8	1/8

Isolation of Toxoplasma

Suspension of brain was inoculated in Sheffield by combined intracerebral and intraperitoneal routes into six mice on 9th December, 1954. Toxoplasms were found in 5 of these mice killed between the eighth and thirteenth day after infection.

Suspension of brain, liver and spleen was inoculated intraperitoneally into eight mice in Edinburgh on 8th December, 1954. Four were taken to Sheffield. These were killed after 12, 42, 82 and 83 days. Toxoplasms were isolated from 3 in first intracerebral and intraperitoneal passage. Second passage mice were inoculated

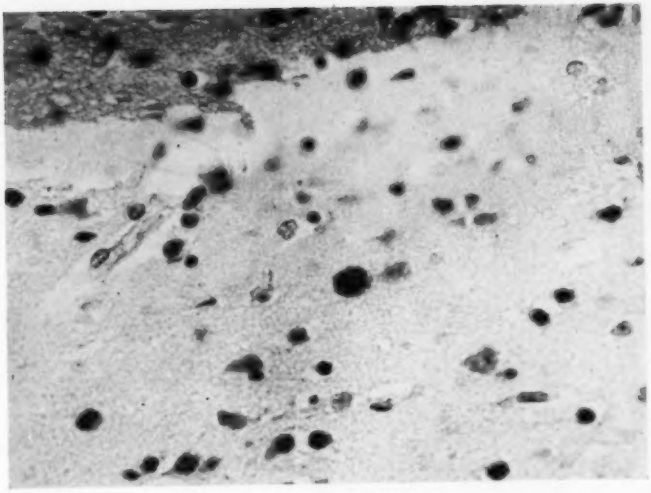

FIG. 1

Case 1. Toxoplasma pseudocysts in apparently healthy brain tissue. ×550.

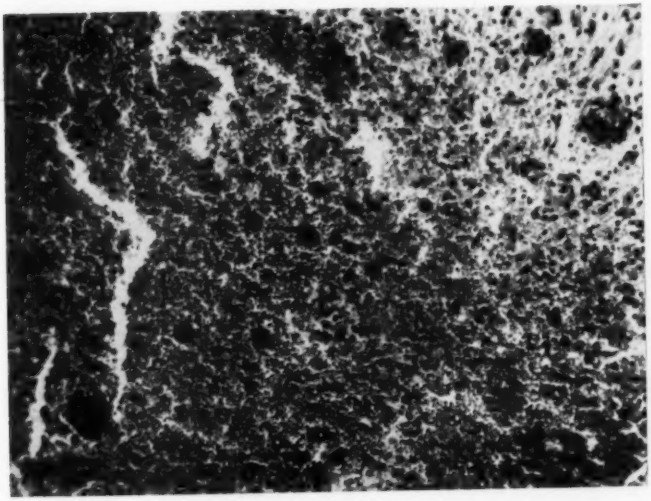

FIG. 2

Case 1. Aggregations of granular material having some resemblance to pseudocysts, but without surrounding membrane. Found in necrotic area of brain. ×125.

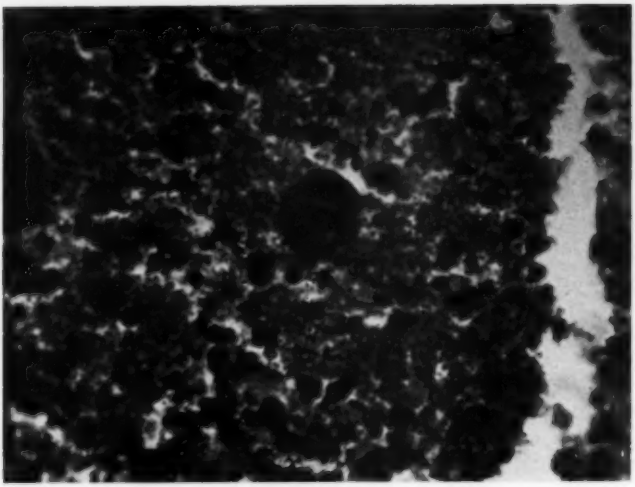

FIG. 3

Case 1. Aggregations of granular material having some resemblance to pseudocysts, but without surrounding membrane. Found in necrotic area of brain. ×600.

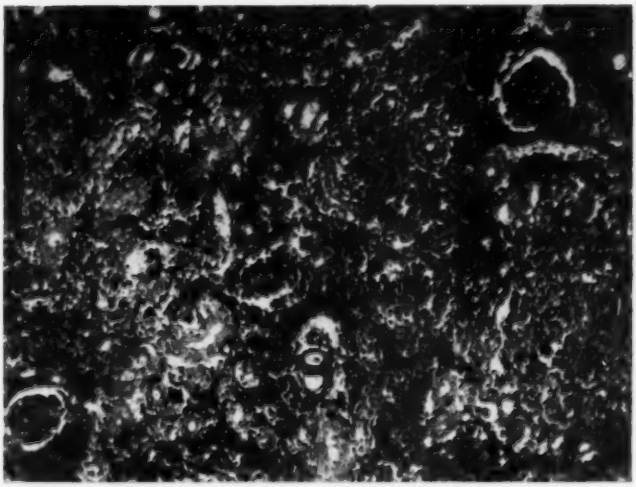

FIG. 4

Case 1. Excessive haemopoiesis in kidney. ×134.

A.D.B., J.H.B., W.F.F., J.K.A.B., C.P.B.

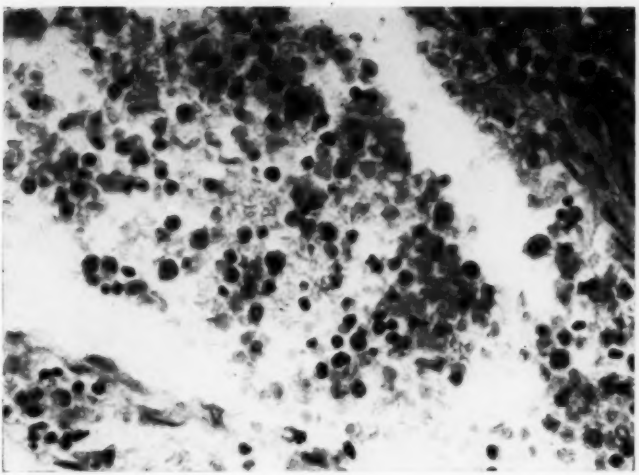

FIG. 5

Case 1. Primitive type of red cells in kidney. ×500.

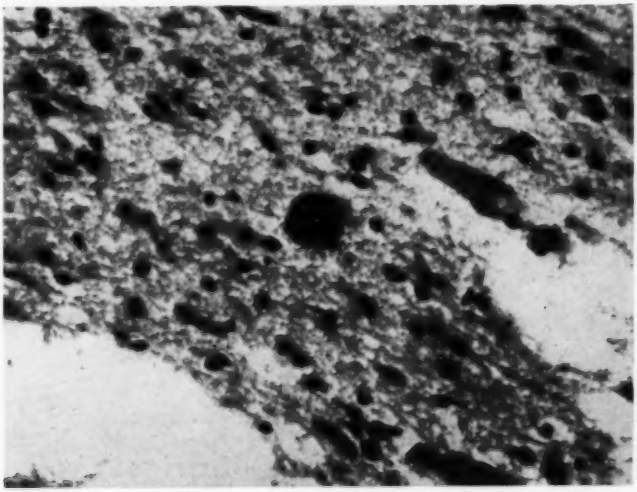

FIG. 6

Case 2. Toxoplasma pseudocysts in brain. ×550.

A.D.B., J.H.B., W.F.F., J.K.A.B., C.P.B.

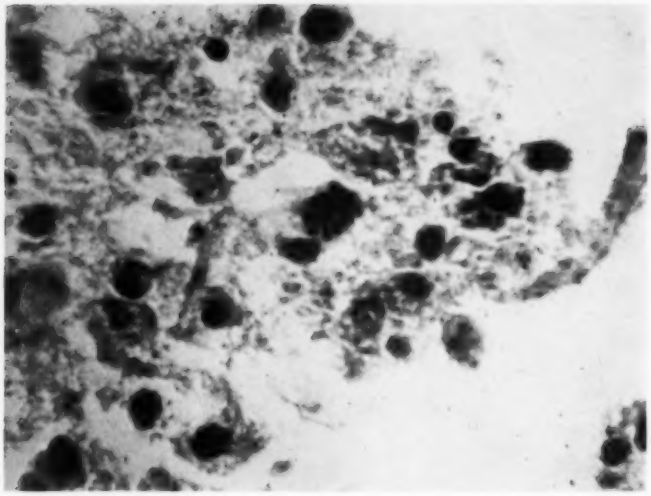

FIG. 7

Case 2. Toxoplasma terminal colony in brain. ×1,100.

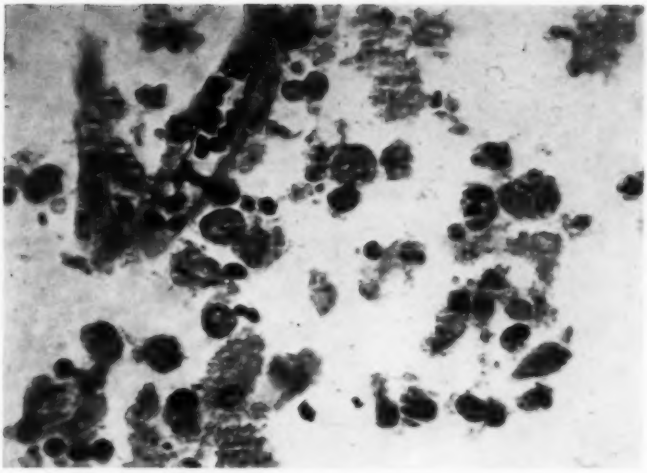

FIG. 8

Case 2. Aggregation of granular material in brain. ×600.

A.D.B., J.H.B., W.F.F., J.K.A.B., C.P.B.

and left for 102 days. Third passage from one of these resulted in death from toxoplasmosis in 10 days.

One of the original mice had a litter of four 44 days after inoculation. These were alive and apparently well 28 days later. They were then killed and one was observed to have an enlarged spleen and increased peritoneal fluid. Neither from this mouse nor its litter-mates were toxoplasms obtained.

Passage was made by the intraperitoneal route alone from the 4 mice retained in Edinburgh. Scanty toxoplasms were found in the passage mice, but two further passages were unsuccessful.

A further 3 mice were inoculated in Edinburgh on 24th December, 1954 with a suspension of the baby's brain, liver and spleen, after it had been kept at 4° C. for 16 days. Toxoplasms were found in the first passage mice inoculated from these.

Unsuccessful attempts were made to isolate toxoplasms by inoculating a suspension of the baby's brain on the chorio-allantoic membrane of fertile eggs.

Case 3. Baby G., born on 23rd August, 1955.

The mother's first pregnancy was in August, 1952, and resulted in abortion at 12 weeks. Her second pregnancy went to term and a normal live baby was born in February, 1954. This, her third pregnancy, resulted in the birth of a stillborn macerated foetus at 30 weeks.

Except for a slight oliguria the mother's health was good during this pregnancy.

Post-mortem Examination

The body was severely macerated with widespread desquamation. The remaining epidermis was deep yellow, but this may have been the result of meconium staining.

When the skull was removed the underlying brain, although extremely soft and macerated, showed ill-defined, yellowish-white areas which were probably either on the surface of the brain or related to the pia-arachnoid. Nothing could be distinguished when the brain was sectioned. It was almost entirely mush. All the serous sacs contained blood-stained fluid. No abnormality was noted in the heart or lungs. The spleen, however, was found to be approximately twice the usual size.

The liver was of normal size. Neither the liver nor spleen gave the Prussian blue reaction.

No pathological changes were found in any other organ.

The placenta was not unusual in appearance.

Histology

Advanced maceration made it difficult to detect any other change in the organs. No calcification was found in the brain.

Serology

Blood Grouping

Mother: Group A Rh. negative.

Father: Group O Rh. positive (probable Rh. genotype CDe/ode).

Previous pregnancy (1954) Baby Group O, Rh. unknown. Coombs's test negative.

Toxoplasma Antibodies

	Dye Test	C.F.T.
Mother:		
25th August, 1955	1/10,000	1/64
Father:		
2nd September, 1955 ..	1/46	

Attempted Isolation of Toxoplasma

Suspensions of placenta, brain, spleen and liver were inoculated into mice and guinea pigs. Some of those inoculated with brain died a few days later of bacterial infection. The rest survived for 2 months. Their sera were then tested for toxoplasma antibodies without significant result. Failure to isolate toxoplasms is attributed to the advanced decomposition of the brain.

Discussion

The laboratory investigations present some points of interest.

Mrs. D.'s serum dye test antibodies rose markedly in titre in the last month of her subsequent pregnancy. Vivell and Buhn (1953) claim that in 10 to 15 per cent of instances pregnancy raises an already existing titre.

The baby then born was found to have passively transferred antibodies to even higher titre than its mother, yet it was and remained perfectly well. High antibody titres alone, even if found both in mother and baby, do not necessarily indicate current toxoplasma infection.

Interesting, but not novel, is the prolonged survival of some of the inoculated animals and their giving birth to healthy offspring. One guinea pig, subsequently proved to be infected, survived for 250 days and had produced a healthy litter. So too, one of the mice had a healthy litter 44 days after inoculation, and was proved to have toxoplasmosis 39 days later. As has been shown by many workers, among them Lépine (1929) and Weinman (1943), toxoplasms may persist in mice without doing any apparent damage for long periods even for the duration of their natural lives. Still more often do they do so in the more resistant rat and guinea pig.

Surveys for antibody suggest that toxoplasma infection is not uncommon in the population of this country (Beverley, Beattie and Roseman, 1954). It is also likely that as in animals the parasite may in some cases persist for long periods. Jacobs, Fair and Bickerton (1954) isolated it from the eye of a man who gave a history of recurrent chorio-retinitis for eight and a half years. Stanton and Pinkerton (1953) found it in an enlarged cervical lymph node of a 26-year old woman who had an illness resembling toxoplasmic lymphadenopathy 5 years before. She gave birth to a healthy infant 36 weeks after the excision of the lymph node.

It would seem reasonable to expect that for a woman to infect her foetus she must have a parasitaemia while the foetus is susceptible. Generally it is assumed that this parasitaemia will be due to recent infection. Very rarely will this infection produce clinical signs in the mother. The only instance known to the authors of proven clinical toxoplasmosis in both mother and baby is reported by Alexander and Callister (1955). The mother had toxoplasmic lymphadenopathy and the baby typical congenital toxoplasmosis with hydrocephalus, enlarged spleen and liver and choroido-retinitis. In addition marked extramedullary haematopoiesis and generalized oedema were noted. Almost invariably the mother's infection will be latent. That parasitaemia can occur in latent infection has been shown by Prior, Cole, Docton, Saslaw and Chamberlain (1953), who isolated the parasite from the blood of a healthy young woman. It is, however, possible that transfer of infection to the foetus may be due not to the parasitaemia of acute infection, but to rupture of pseudocysts of chronic infection as suggested by Weinman (1952) and by Mellgren, Alm and Kjessler (1952). The difficulty in accepting the latter suggestion is that subsequent children do not have congenital toxoplasmosis.

The period during which the foetus is susceptible is probably long. It is unlikely to be in the first few weeks when the parasite would be dissolved by the enzymatic action of the trophoplast. In the case reported by Gard and Magnusson (1951) infection immediately prior to or shortly after the onset of pregnancy was followed by the birth of a healthy infant.

Infection of the mother at a somewhat later stage has led to abortion. Magnusson (1951) isolated the parasite from a foetus aborted at the third month. As the mother's dye test titre rose from 1/40 at that time to 1/250 five weeks later it is presumed that she was infected early in pregnancy. (Toxoplasmosis would not, however, appear to be a common cause of abortion. Feldman and Eichenwald (Sabin, 1953) failed to find serological evidence of current toxoplasmosis in any of 95 women who aborted.) The mother, whose case is reported by Alexander and Callister (1955) and already quoted, developed lymphadenopathy when 6-months pregnant. Heath and Zuelzer (1945) consider, on account of the nature of the eye lesions, that the twins they describe were infected not later than the seventh month of intra-uterine life. That toxoplasmosis may not manifest itself in the baby until some days or weeks after birth suggests that infection may sometimes occur in the last month of pregnancy.

There is much evidence that toxoplasma can damage the vascular and haemopoietic system, but how it does so is not clear.

Among the earliest cases reported were the 2 in adults described by Pinkerton and Henderson (1941). In these there was a rash stated to resemble that of typhus. More recently Giroud, Jadin and Reizes (1951) have produced evidence that some cases of exanthematic fever in the Congo are due to toxoplasma. In such cases, as in typhus, it is possible that toxoplasma invades the endothelial cells lining the walls of the capillaries and so produces thromboses.

Pinkerton and Henderson (1941) did, indeed, find in the brain of their cases pericapillary lesions resembling those of typhus.

In congenital cases rashes have been frequently reported: Zuelzer (1944), Callahan, Russell and Smith (1946), Wyllie, Fisher and Cathie (1950), Riley and Arneil (1950), Sabin *et al.* (1952), Hall *et al.* (1953), Magnusson and Wahlgren (1948), Beckett and Flynn (1953), and Morris, Levin and France (1955).

The rash has been variously described as purpuric, maculo-haemorrhagic, maculopapular. Here again there may have been capillary damage or a reduction in platelets, or prothrombin deficiency. The last has been recorded by Magnusson and Wahlgren (1948) and by Gard, Magnusson, Wahlgren and Gille (1949).

Bleeding has also been reported into the skin (Smitt and Winblad, 1948), from the umbilical cord and lip (Silver and Dixon, 1954), in the stomach, intestine and lung (Callahan, Russell and Smith, 1946).

Several authors have noted a resemblance to haemolytic disease of the newborn (Callahan, Russell and Smith, 1946; Magnusson and Wahlgren, 1948; Harwin and Angrist, 1948; Neiditsch, 1951; Beckett and Flynn, 1953; Hall *et al.*, 1953), and the present authors have encountered one case the most prominent feature of which was severe thrombocytopenic purpura at one day of age.

It would be satisfactory to be able to relate this to specific damage caused by toxoplasma to the blood forming organs. The frequency of jaundice would suggest liver damage, but only rarely can evidence of this be found histologically. Nor in spite of observations of the presence of toxoplasma in bone marrow (Pinkerton and Weinman, 1940; Kabelitz, 1952; Finckh, 1954) does damage to this tissue appear to be the cause.

For the present at least it must be left as an instance (cytomegalic inclusion disease is another (Colebatch, 1955)) of extra-medullary erythropoietic activity produced by a generalized infection.

It would seem worth while to examine for toxoplasma infection cases which appear to be haemolytic disease, but in which no blood group incompatibility between mother and offspring is found. The mother's and baby's sera should be examined for toxoplasma antibodies by the dye test of Sabin and Feldman and by the complement fixation test. If the baby has died a suspension of its brain should be inoculated into mice. This should not be dismissed as impracticable because mice are not immediately available since toxoplasms survive for 16 days in brain tissue kept at 4° C.

It would be of interest and perhaps of importance to take note of any illness, however mild suffered by the mother during pregnancy. Experience at present suggests that glandular enlargement may be the commonest manifestation of acquired toxoplasmosis.

Summary

Three cases of congenital toxoplasmosis are reported.

All three had greatly enlarged spleens; two had enlarged livers. One was macerated and another presented the picture of hydrops foetalis.

Attention is drawn to the resemblance congenital toxoplasmosis may bear to haemolytic disease of the newborn.

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FURTHER OBSERVATIONS ON THE PROGNOSIS IN TOXAEMIA OF LATE PREGNANCY

BY

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IN a previous paper (Gibson, 1954) the immediate prognosis in toxaemia of late pregnancy was discussed on the basis of a series of 1,420 patients who had toxaemia and were delivered in the Royal Maternity Hospital, Belfast, during the years 1946–50 inclusive. In this series the onset of toxaemia was not regarded as an absolute indication for the immediate termination of pregnancy. Special reference was made to the practice of selective continuation of such pregnancies with the object of improving the foetal prognosis by the resulting gain in foetal maturity at the time of delivery. It was shown that, providing an imminent risk of eclampsia was not ignored, the immediate maternal prognosis did not deteriorate as the result of continuation of a toxaemic pregnancy. No opinion was expressed concerning the later effects of this "conservative" treatment. This is a point of great importance but when one refers to the literature for guidance it is apparent that there are two opposing schools of thought.

Gibberd (1934) considered that pre-eclamptic toxaemia predisposed a patient to chronic nephritis and that early induction of labour reduced the incidence of this complication. It is probable that he referred to nephrosclerosis and there are few today who consider chronic nephritis as a sequel to pre-eclamptic toxaemia; many, however, hold that chronic hypertension is a sequel and this view gains particular support in the United States of America. Peckham (1941) followed up a series of 500 cases of pre-eclamptic toxaemia and came to the conclusion that, if four weeks of conservative treatment were exceeded, there was a great increase in the incidence of residual hypertension. A possible fallacy in his findings is the fact that the diagnosis of pre-eclamptic toxaemia was made in any patient who had previously had three normal blood pressure and urine examinations during her attendance at the antenatal clinic. As many hypertensive patients have a drop in blood pressure during the middle trimester, these patients may have been erroneously diagnosed as cases of pre-eclamptic toxaemia. Such patients are likely to require admission to hospital at an earlier stage in pregnancy than the normotensive patients and are thus more likely to receive weeks of conservative treatment. Chesley, Somers and Vann (1948) followed up 242 cases and concluded that the radical treatment of pre-eclamptic toxaemia undoubtedly reduced the incidence of residual hypertension. Lewis (1940) held the same view while Dexter and Weiss (1941) stated that permanent hypertension was proportional to the duration rather than to the severity of toxaemia. Kellar (1939) considered that the woman destined to develop hypertension in later life was peculiarly liable to develop pre-eclamptic toxaemia and that this toxaemia might hasten the onset and progress of essential hypertension. McKelvey (1955) when discussing the 10-year prognosis after pregnancy, states "a good statistical case can be made for the fact that one disease alone, arteriosclerosis or essential hypertension or nephrosclerosis or whatever you wish to call it, initiated clinically as a pregnancy toxaemia will produce in mortalities alone somewhere between five and ten times the total deaths due to all other causes of immediate maternal mortality combined".

The view that pre-eclamptic toxaemia does not predispose a patient to chronic hypertension is supported by the classical papers of Theobald (1933), Isenhour, Kuder and Dill (1942), and Barnes and Browne (1945). The last paper was based upon the blood pressure findings in 915

nulliparous and 1,041 parous patients attending a gynaecological clinic. Briefly, these writers found no statistical difference in blood pressures between the nulliparous and parous patients age for age. There are objections to the conclusion that this proves that pre-eclamptic toxaemia does not predispose to chronic hypertension. Firstly, the age groups (10 years) were rather large and an increased tendency to hypertension in parous patients might well be lost in the averages. Secondly hypertensive patients, by dying, may have excluded themselves from the parous group. Thirdly, introspective nulliparae who attend a gynaecological clinic may, as a class, show an undue tendency to hypertension and may not therefore serve as a satisfactory control group. Lastly, the conservative treatment of pre-eclamptic toxaemia was frowned upon at the time that the parous patients in the series had their pregnancies. Therefore comparable blood pressures in the parous and nulliparous groups do not prove that conservative treatment can be exonerated as a cause of chronic hypertension—none of the parous patients may have been treated conservatively.

Dieckmann (1952, p. 635) states: "Since 1933 I have believed that pre-eclampsia/eclampsia rarely causes vascular or renal pathology and, in general, that the patient who had such pathology would have had it eventually if she had never been pregnant." Tillman (1955) reviewed a series of 240 primigravidae in whom the pre-pregnant blood pressure was known to be normal. At review 6·6 per cent were hypertensive, the percentage being the same whether pregnancy had been normal or toxaemic. Unfortunately these blood pressures were supplied by numerous observers and were presumably recorded under widely differing circumstances. They were also recorded at varying times before pregnancy started so that there are several factors which could have affected the results. It is all too easy to be critical of clinical investigations because patients are subject to so many variables which may upset statistical interpretations. Nevertheless it is only by clinical research that the risks associated with toxaemia of pregnancy may be estimated and the writer wishes to present the results of an investigation which was completed in 1954.

The Investigation

There were 1,420 toxaemic pregnancies in the Royal Maternity Hospital, Belfast, during 1946–50. In 1951 it was decided to review all these cases in order to collect data about later prognosis and, for this purpose, a special clinic was started. All the patients were invited to attend this clinic and they were interviewed by the writer or by Professor Macafee. Their blood pressures were recorded when they were lying comfortably on a couch and catheter specimens of urine were examined for albumen and sugar. In passing, it was interesting to note the number of patients who desired advice during this interview or had some disability requiring treatment such as chronic cervicitis, diabetes or obesity.

Naturally a considerable number of patients failed to attend the clinic. If these patients resided in N. Ireland they were traced to and examined in their own homes. If they had moved abroad, the clinic card was sent to them with an invitation to have it completed by their family doctor. A word of appreciation should be expressed to the 41 patients and their doctors who have helped in this way—Patna, Istanbul, Vancouver, Bulawayo and Christchurch are just five of the places from which cards have been returned.

When the follow-up had been completed it became apparent that 1 patient had 4 pregnancies, 5 had 3 and 50 had 2 pregnancies included in the series. Of the total of 1,420 pregnancies in the series 1,358 were followed up (95 per cent) this representing 1,295 patients (94·7 per cent). There were 62 patients who were not reviewed, the reasons being as follows:

(*a*) 12 were unmarried girls.
(*b*) 22 had moved abroad and failed to supply the information for which they were asked.
(*c*) 28 could not be traced.

Hypertension and nephritis are progressive conditions and it is therefore of considerable consequence to define the stage at which patients were followed up after pregnancy. In this investigation an attempt was made to review patients 4 years after confinement and this represented the average. Inevitably a few were seen sooner and others later, the minimum being 2½ years and the maximum 7 years.

Re-classification

Toxaemia of late pregnancy is a collective term which includes four separate disease entities, pre-eclamptic toxaemia, eclampsia, chronic hypertension and chronic nephritis. In the previous paper cases were classified according to the criteria discussed by Browne (1946, p. 396) and no less than 53·7 per cent defied classification because the clinical history was equivocal or a record of the blood pressure and urinary findings before the twentieth week of pregnancy was not available. This was a most unsatisfactory state of affairs and, when the review had been completed, an attempt was made to reclassify these cases. The results of this re-classification are shown in Table I and the original classification has been included for comparison. It will be noted that 309 cases (22·8 per cent) still defy classification. Sixty of these probably had pre-eclamptic toxaemia and chronic hypertension was the most likely diagnosis in 167 cases. It proved quite impossible to place any label on the remaining 82 cases.

Table I
Classification of Cases
(Percentages)

	Original Series	Re-classification
Pre-eclamptic toxaemia and eclampsia	37·4	63·6
Chronic hypertension	7·5	11·7
Chronic nephritis	1·4	1·9
Unclassified	53·7	22·8

Maternal Prognosis

There were 31 maternal deaths in the series. Four of these were described in the previous paper and in the remainder the cause of death is shown in Table II. Only one patient who had been diagnosed as suffering from pre-eclamptic toxaemia subsequently died of hypertension. On going through her history again it was discovered that she had had an extended lumbo-dorsal splanchnicectomy before her pregnancy so that the diagnosis was in error.

Only a few of the patients were found to have albuminuria during the review. Their co-operation was seldom found to include a willingness to be admitted to hospital for full renal examinations. However, it may be confidently stated that, in so far as albuminuria may be considered as an essential finding in nephritis, pre-eclamptic toxaemia does not predispose to chronic nephritis.

Table II
Maternal Mortality

Cause of Death	Number of Cases
Hypertension	10
Nephritis	3
Cancer	4
Heart disease	3
Accident	3
Asthma	1
Phthisis	1
Pneumonia	1
Lung abscess	1
Total	27

In assessing the risk of chronic hypertension several problems arise. Firstly the prognosis will naturally depend upon the type of toxaemia from which the patient suffered during her pregnancy. Although all were reviewed and it must be emphasized that the original diagnosis was not known during the patient's examination, the prognosis will only be discussed in relation to patients who were "correctly" diagnosed as suffering from pre-eclamptic toxaemia in the original classification. It must be mentioned that, in a number of cases, the marked degree of hypertension at review cast some doubt upon the rectitude of this diagnosis. One of the criteria for diagnosis was the record of a normal blood pressure before the 20th week of pregnancy. Browne (1947) and Kellar (1955, p. 230) have drawn attention to the fall in blood pressure which occurs in hypertensive patients during the middle trimester of pregnancy. This fall may occur well before the 20th week of pregnancy and may lead to an erroneous diagnosis of pre-eclamptic toxaemia in patients suffering from chronic hypertension. Secondly, there is no measure of agreement as to what level of blood pressure should be considered as evidence of chronic hypertension. Master, Dublin and Marks (1950) investigated the maximum level of blood pressure which should be considered as

normal in women at various ages. They concluded that the maximum should be 140/90 at 20–24 years and 175/105 at 45–49 years. Such a sliding scale complicates any assessment and for the purpose of this investigation any patient with a blood pressure of 140/90 was considered to have hypertension. If either the systolic or diastolic pressure was below this critical level the patient was considered to be normotensive. Lastly, some patients had further pregnancies before their review and it is possible that these pregnancies had some influence on their blood pressures. A case could be made out for their inclusion and, rightly or wrongly, the writer decided against any further exclusions from the 434 cases of pre-eclamptic toxaemia out of the 1,358 pregnancies which were followed up—the reduction is very large already and underlines the disheartening aspect of clinical research into this problem.

There were 131 patients who were found to have hypertension after pre-eclamptic toxaemia, an incidence of 30·2 per cent. Light (1948) and Dieckmann (1952, p. 580) report an incidence of 30 per cent and 29 per cent respectively but Kellar (1955, p. 240) states "it can be taken for a fact that about 50 per cent of all women suffering from pre-eclampsia will develop essential hypertension in the years that follow". Comparison with the experience of others is of doubtful value, however, because so much depends upon the time that elapses before review and also upon the level of blood pressure which is accepted as evidence of hypertension. Comparison within the series is of greater value and the effect of "conservative" treatment on the incidence of hypertension is shown in Table III. In this table the cases were divided into the same three groups as in the previous paper, this division depending upon the duration of toxaemia, i.e., the duration of "conservative" treatment in hospital before delivery. It will be seen that 25·8 per cent of the patients who were delivered within 7 days of admission to hospital had residual hypertension. When toxaemia persisted for 14 days, or more, the incidence increased to 32·8 per cent. This difference in percentage is not statistically significant ($\chi^2=2{\cdot}90$ and $P>0{\cdot}20$) and the findings strongly support the view that prolongation of a toxaemic pregnancy does not increase the risk of residual hypertension. It may be argued that the findings in Table III are inconclusive because toxaemia must persist for 28 days before permanent damage occurs. However, there were 39 patients who did have toxaemia for more than 28 days. The incidence of residual hypertension was 28·2 per cent in this group, a figure which does not support such a contention.

TABLE III
Residual Hypertension
(Related to duration of treatment)

	No. of Cases	Residual Hypertension	Percentage
Total cases*	434	131	30·2
Less than 7 days treatment	190	49	25·8
7–13 days treatment ..	125	43	34·4
More than 13 days treatment	119	39	32·8

* Cases of pre-eclamptic toxaemia only.

It has been widely held in the past that the severity of toxaemia influences the incidence of residual hypertension, and in particular, that mild cases are more prone to become hypertensive later. In Table IV the cases have been grouped according to the severity of toxaemia and again there is no significant difference between the groups as regards the incidence of hypertension. Light (1948) reviewed 391 pre-eclamptic patients and he also concluded that the severity and the duration of toxaemia had no influence on the ultimate prognosis. He correlated the incidence of residual hypertension with the patient's age and this revealed a direct relationship—at 20 the incidence of residual hypertension was 13·1 per cent and, over 35, the incidence had risen to 52·4 per cent. Table V illustrates the influence of the patient's

TABLE IV
Residual Hypertension
(Related to severity of toxaemia)

Severity of Toxaemia	No. of Cases	Residual Hypertension	Percentage
Mild	180	45	25·0
Moderate	211	72	34·1
Severe	43	14	32·6

TABLE V
Residual Hypertension
(Related to age)

Age at Time of Review	No. of Cases	Residual Hypertension	Percentage
20–24 years	26	3	11·5
25–29 years	145	26	17·9
30–34 years	121	36	29·8
35–39 years	64	25	39·1
40–44 years	61	30	49·2
45–49 years	17	11	64·7

age on the incidence of hypertension in this series. It underlines the supreme effect of age on prognosis. Indeed, in whatever way the review of this group of 434 cases of pre-eclampsia is considered, increasing age appears to be the only factor of importance in prognosis. It suggests that the management of a case of pre-eclamptic toxaemia should only be influenced by consideration of the immediate maternal and foetal prognosis, the later prognosis being ignored with safety—this is in agreement with the views of Browne and Dodds (1939) and Bryans and Torpin (1949).

Ninety patients who were originally classified as cases of chronic hypertension have been reviewed. When the blood pressure at review was compared with the blood pressure in early pregnancy 35·5 per cent had a definite increase in the degree of hypertension. This incidence is less than that reported by Reid and Teil (1939). Leishman (1953) reviewed a group of hypertensive patients approximately 3 years after their first visit to his medical clinic. As 60 per cent of these showed a deterioration at the time of review the lower incidence in this series suggests that pregnancy does not have any deleterious effect on prognosis. The numbers are rather small to assess the effects of conservative treatment on the prognosis—deterioration of the hypertension occurred in 30 per cent of patients delivered within a week of admission to hospital and in 40 per cent of those who had at least 14 days conservative treatment before delivery.

OBSTETRIC PROGNOSIS

During the review all patients were asked for details of any further pregnancies. They showed a surprising lack of knowledge as to what had happened in these pregnancies and, for this reason investigation was limited to a study of the pregnancies for which records were available. The writer is grateful to the Medical Staff of the Jubilee Maternity Hospital, Malone Place Hospital and the Royal Maternity Hospital for allowing him to have access to these records. It may be argued that this selection of cases is bound to give a biassed picture because patients developing toxaemia again will inevitably find their way to hospital while unaffected patients will be confined at home. This is true to only a limited extent, however, because the hospitals concerned follow the practice of booking patients with a history of toxaemia and, in addition, a high percentage of the women of Belfast expect to have all their confinements in hospital.

There were 116 women who had pre-eclamptic toxaemia in their first pregnancy and subsequently had a confinement in one of the three hospitals which have been mentioned. The toxaemia recurred in 43 (37·1 per cent), a percentage which is much less than that quoted by Gibberd (1944). Eighteen had a second pregnancy, 7 developing toxaemia while 2 patients had 3 pregnancies without showing any recurrence of toxaemia. There were 18 patients with chronic hypertension and 15 developed toxaemia in a subsequent pregnancy. The 6 patients who had chronic nephritis all showed an exacerbation of the condition during subsequent pregnancies —one who knew this very well postponed her first attendance at the hospital until a later stage in each of the 4 subsequent pregnancies, so that she could reduce the duration of her antenatal supervision in hospital. She died in 1951 shortly after her fifth confinement, 4 of which were included in the series. This patient was of particular interest. In each pregnancy full investigation appeared to confirm a diagnosis of chronic nephritis and the findings showed a progressive deterioration. However, at post-mortem examination, the patient was found to have an extensive old-standing chronic pyelonephritis. There was also evidence of chronic glomerulo-nephritis but the kidneys were so disorganized that the primary lesion could not be determined. On only one occasion, and that in the first pregnancy, was there a transient

episode of urinary infection which was detected clinically.

Another aspect of the obstetric prognosis became apparent during the review, namely the number of patients who wilfully avoided further pregnancies. In order to assess the frequency of this attitude a selection was made of all patients in the series, who had an adequate chance of becoming pregnant again before they returned for review. The standards for this selection were as follows: (*a*) patients must be less than 35 years of age at the time of review—this age limit was chosen, arbitrarily, in order to ensure that patients retained a reasonable level of fertility; (*b*) an adequate interval, 4 years, should have elapsed after the toxaemic pregnancy before the patient was reviewed.

The findings in this selected group of patients are shown in Table VI. No less than 111 patients

TABLE VI
Obstetric Prognosis
(Selected Group)

Number of Cases	Number Pregnant again	Number not Pregnant again
346	235 (67·9 per cent)	111 (32·1 per cent)

(32·1 per cent) had not become pregnant again before they returned for review. Of this number 22 gave a definite social or economic reason for avoiding pregnancy. A few of the remainder had desired another pregnancy but the majority stated that they had avoided pregnancy for all or part of the time. Their reasons may be summarized under two headings: (*a*) on medical advice, (*b*) because of fear.

The patients who avoided pregnancy on medical advice had received this advice before their discharge from hospital or at their postnatal examination. To many this advice was causing considerable hardship and when reference was made to the details of their pregnancies there seemed to be little reason why this advice should have been given. Because the final resolution of hypertension and albuminuria after a pre-eclampsia may take up to 2 years (Browne, 1946, p. 378) there is a tendency to advise against pregnancy during this time. Such advice underlines the "ordeal" which the patient has been through and, if she is anxious by nature, it may be taken as an everlasting bar against further pregnancy. Although the avoidance of pregnancy may be advisable in certain cases of chronic nephritis and chronic hypertension there appears to be no valid reason for the avoidance of a further pregnancy after pre-eclamptic toxaemia even while hypertension or albuminuria persist. Indeed one patient in the series had her first pregnancy terminated at 24 weeks because of fulminant pre-eclamptic toxaemia. When she returned for postnatal examination 8 weeks later she had started another pregnancy. Hypertension and albuminuria were still severe but the pregnancy was permitted to continue. Resolution of these signs was not complete until the 28th week in this second pregnancy but, subsequently, the pregnancy progressed normally with a successful outcome.

The patients who were afraid to have another pregnancy gave many reasons for their fear. A few gave the impression that their main desire was to avoid another spell of "conservative" treatment in hospital with the disruption of home life which this entailed—in this view they may have been supported by the more selfish type of husband. Others had been seriously ill during their pregnancy. They were often willing to try again but stated that their husbands would not allow them to take the risk. In the remainder the writer formed the opinion that a lack of satisfactory explanations to the patient during her stay in hospital formed the basis of her fear. An extreme example may serve to illustrate this point. A patient attends the antenatal clinic and is admitted to hospital at short notice although she feels perfectly well. She lies in the antenatal ward for some time without any apparent treatment. She receives an anaesthetic for the induction of labour. Far from finding that her baby has been born when she awakes she has to return to the antenatal ward for another few days. There are attempts at hastening the onset of labour by enemata and Pitocin injections. When labour does start her state of anxiety causes uterine inertia, a long labour and operative delivery. The condition of the baby causes anxiety and the mother does not see the baby until any hope of establishing breast

feeding has passed. If she receives this treatment at the hands of several doctors with no sense of continuity her rout is complete. This aspect in the management of toxaemic patients does not arise in private practice and, if thought is given to it, should not cause difficulty in hospital practice.

Foetal Prognosis

There were 84 sets of twins and 2 sets of triplets in the series so that 1,358 confinements provided a total of 1,446 babies. It will be seen in Table VII that the immediate foetal mortality

Table VII
Infant Prognosis

	Number	Percentage
Immediate deaths	237	16·4
Later deaths	29	2·0
Living children	1,180	81·6
"Backward" children ..	7	—

was 16·4 per cent and that 29 babies (2 per cent) died subsequently. It was felt that 3 of these deaths were definitely attributable to toxaemia. In these 3 cases the babies were immature and barely survived the neonatal period. In the remainder the deaths occurred between the ages of 1 month and 5 years. Baird, Thomson and Duncan (1953) report infant mortality rates (one month to one year) which varied from 12 to 37 per 1,000 in Aberdeen during the years 1946–50. These figures are not strictly comparable with the 2 per cent mortality in this series because this mortality extends beyond the end of the first year. However, the comparison does suggest that, if a toxaemic mother is delivered of a living child, and the child survives the neonatal period, subsequent progress should follow the normal pattern. Mention must be made of 7 children who were "backward", 3 being mentally defective and 4 spastic. All of these children had operative deliveries and 3 were also very premature at birth. It is possible that the maternal toxaemia may have been a contributory factor in these cases in that it stimulated the accoucheur to interfere where, otherwise, he would have awaited a normal delivery.

Summary

(1) In a previous paper the immediate prognosis in toxaemia of late pregnancy was discussed on the basis of a series of 1,420 patients who were delivered in the Royal Maternity Hospital, Belfast, during 1946–50.

(2) From 1951–54 an attempt was made to review all these patient in order to obtain information about the later prognosis. This review was 95 per cent successful.

(3) There were 434 patients who had been diagnosed as suffering from pre-eclamptic toxaemia. When a blood pressure of 140/90 was used as a standard, 131 of these patients (30·2 per cent) had residual hypertension.

(4) Neither the duration nor the severity of the toxaemia played any part in the production of residual hypertension, the age of the patient being the only factor of importance.

(5) The records of further pregnancies were available for 116 women who had had pre-eclamptic toxaemia—37 per cent again had toxaemia.

(6) It was found that a considerable number of patients had avoided further pregnancies and their reasons were discussed.

(7) Providing that the children of these toxaemic pregnancies survived the neonatal period their further progress appeared to be satisfactory.

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ECLAMPSIA IN THE ABSENCE OF CONVULSIONS, COMA OR ALBUMINURIA

("Eclampsia sine eclampsia" in two sisters)

BY

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J. P. GREENHILL (1947) (in Joseph B. De Lee's *Principles and Practice of Obstetrics*) shows as an illustration of eclampsia a coloured photograph of a liver. It is of interest to note that this picture has been taken from the case of "eclampsia without convulsions, hypertension, or coma" reported by Reis and Bernick (1944).

It has been stated that the prognosis in eclampsia deteriorates with the increase in the number of fits. In cases where fits are absent and coma arises early, the outlook is even worse. The cerebral cortex is no longer irritable but has been put out of action altogether. There is yet another type of eclampsia, without fits, also mostly fatal, in which circulatory collapse predominates (Held, 1948).

In all these forms typical pathological changes were found on post-mortem examination of the liver.

A number of cases of eclampsia without convulsions have been reported; but the absence of convulsions, coma and albuminuria and the presence of only minimal hypertension appears to be exceedingly rare.

Case History of Mrs. G.M.

Mrs. G.M., a primigravida, aged 25, booked up at the antenatal clinic when she was 3 months pregnant. She had not suffered any previous illness except rubella. On general examination no important abnormality was discovered.

Her pregnancy progressed uneventfully. The relevant antenatal observations are recorded in Table I.

She was admitted in labour at 7.30 a.m. 4 days after the last attendance at the antenatal clinic, stating that labour had started at 4 a.m. that morning. Her general condition was good, temperature 98·6° F., pulse 92, respiration 20, blood pressure 130/90, urine normal. The vertex was engaged, the membranes were intact, uterine contractions were only fair, recurring every 6 minutes. The foetal heart rate was 134. At 10.40 a.m. the cervix was 3–4 fingers dilated, an enema was given and afterwards an intramuscular injection of 100 mg. of Pethidine. The cervix was fully dilated at 2 p.m. After a second stage of 1 hour 25 minutes the patient delivered herself of a healthy male child weighing 7 pounds 10½ ounces following episiotomy by the house surgeon. There was a blood loss of 10 ounces before delivery of the placenta. The third stage was completed after 25 minutes, but the delivery of the placenta was accompanied by a further blood loss of 20 ounces at 3.50 p.m. This was treated by intramuscular injection of 0·5 mg. of ergometrine.

Table II indicates the progress following delivery.

TABLE I

Duration of Pregnancy	Weight	Blood Pressure mm. Hg	Urine, Albumen, Sugar	Remarks
14 weeks	8 stone 1 pound 12 ounces	114/60	Nil	
32 weeks	9 stone 9 pounds	110/74	Nil	
34 weeks	9 stone 9 pounds 4 ounces	124/74	Nil	
36 weeks	9 stone 13 pounds 4 ounces	118/70	Nil	
37 weeks	Not recorded	142/90	Nil	Advised rest and salt-free diet.
38 weeks	10 stone 1 pound 7 ounces	130/90	Nil	

TABLE II

Time	Pulse Rate	Blood Pressure	Remarks	Treatment
p.m. 3.50			Completion of 3rd stage of labour, total blood loss 30 ounces.	Ergometrine 0·5 mg. intramuscularly.
4.00	132			
4.15	132	110/88		Repair of episiotomy (28 ml. of "xylocaine")
4.30			Further blood clot expressed (10 ounces).	Ergometrine 0·5 mg. intramuscularly.
5.00	160	95/70	Cold, drowsy, moderately shocked.	
5.15	120		Better colour, warm.	Transfusion with "Dextraven"; Omnopon gr. ½.
6.00	112	112/86		
7.00	140	98/50		Total of 47 ounces of "Dextraven" transfused. Drip continued with saline.
8.00	156	110/60	Temperature 100·6° F. Good colour. Detailed general examination showed no abnormality. No further bleeding.	Omnopon gr. ½.
8.30	120		Sleeping.	
8.55	124		Answering questions.	Transfusion changed to blood.
9.00			Collapsed and died a few minutes later.	Coramine, oxygen, artificial respiration.

POST-MORTEM FINDINGS

(Examination carried out 60 hours after death)

Liver (Figs. 1 and 2)

The rather large liver, with a tongue-like extension of the left lobe, had on its smooth pale brown external surface numerous areas of irregularly-shaped and poorly delimited carmine red petechial haemorrhage (largest, approximately 6 cm. diameter). The yellow-brown cut surface bulged slightly and the normal lobular architecture was obliterated, the small vessels in the portal tracts being unduly conspicuous owing to their apparent dilatation and the bright red blood in their lumina. Dissection of the portal and hepatic veins and portal artery showed no abnormality of their larger branches.

On microscopic examination (Figs. 3 and 4), there was haemorrhage into the connective tissue of most of the portal systems, and in many of them the haemorrhage extended out into the peripheral zone of the liver lobule, where it was accompanied by degeneration and necrosis of liver cells; the amount of liver tissue destroyed was, however, small. The liver cells not involved by the haemorrhages appeared fairly healthy, but there was considerable disintegration of the liver-cell columns. The histological picture seemed to be essentially the same as that which is characteristic of eclampsia though the amount of haemorrhage in the portal systems was greater, and that actually in the liver parenchyma less, than usual.

FIG. 1

FIG. 2

Eclamptic liver. There are numerous irregularly-shaped subcapsular haemorrhages. On the yellow-brown cut surface the vessels in the portal tract are unduly conspicuous.

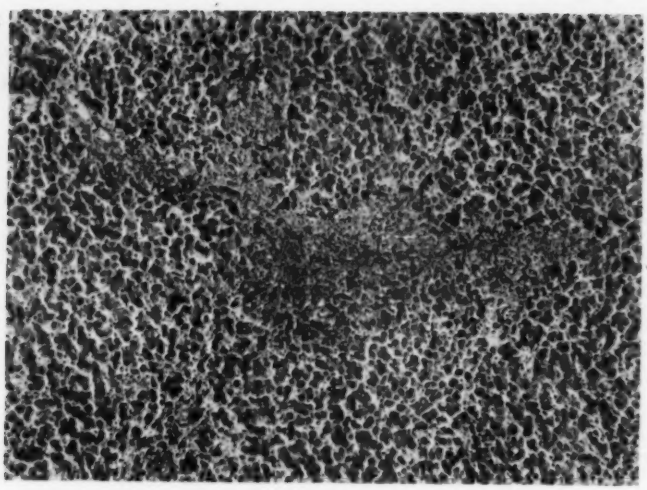

FIG. 3

There are haemorrhages in the portal tracts, spreading into the peripheral zone of the liver lobules. ×80.

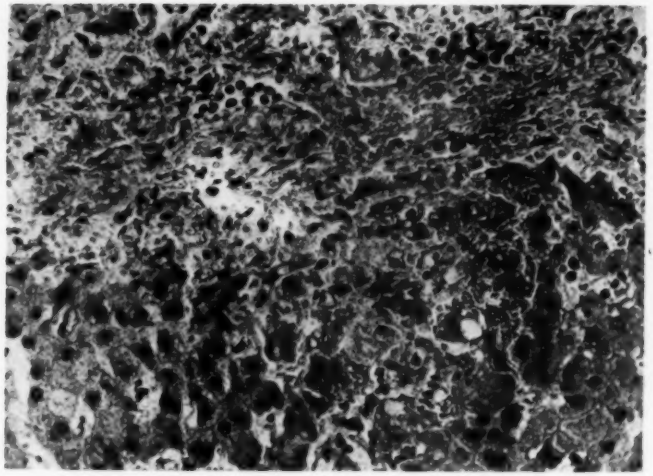

FIG. 4

High power view of a portal tract with two bile canaliculi. There is haemorrhage in the portal tract and degeneration and necrosis of liver cells in the peripheral zone of the adjacent liver lobules. ×300.

Kidneys

These were slightly enlarged and had a conspicuous zone of congestion in the outer medulla on their pale cut surfaces. The capsules stripped easily, leaving a smooth subcapsular surface. The cortico-medullary ratio was normal (average width of cortex 0·7 cm.). Arcuate vessels were not unduly conspicuous. Dissection of renal arteries and veins into the hilum of the kidney revealed no abnormality. The renal pelves were somewhat dilated and there was conspicuous dilatation of both ureters down to the pelvic brim.

Microscopically, there was probably a slight increase in cellularity and undue stiffening of the basement membranes of the renal glomeruli, but neither of these changes was very definite. There was hyaline droplet degeneration of the epithelial cells of the tuft in a few glomeruli, and an excess of polymorphonuclear leucocytes in their capillaries. The epithelium of the proximal convoluted tubules was necrotic in many areas of the cortex, the affected cells being vacuolated and devoid of nuclei. In the intervening parts of the cortex the proximal convoluted tubules appeared relatively normal. Desquamation of epithelial cells was present in the distal convoluted and collecting tubules: their nuclei still stained well even when the cells were completely detached from the basement membrane. Much yellow-brown pigment was seen in the epithelium of many tubules.

Heart and Great Vessels

The heart was opened under water and did not show any air embolus. The pulmonary artery contained post-mortem clot only. The intra-pulmonary branches of the pulmonary artery and vein were normal. The great veins and their tributaries contained no ante-mortem thrombus or air and were normal in distribution.

Lungs

The lungs showed poor aeration and, on microscopic examination, considerable collapse, especially in the lower lobe sections.

No relevant abnormalities were found in other organs.

The autopsy finding of eclampsia came as a complete surprise, for the only finding suggestive of toxaemia since admission had been a blood pressure of 130/90. The failure to make a correct ante-mortem diagnosis prompted the author to discuss the clinical features of this case for they had given very little indication of an underlying toxaemia of such considerable gravity.

Discussion

(a) *Weight Gain*

The total weight gain from the time when the patient was first seen, i.e., at the 14th week, to the 38th week was 28 pounds. This is, according to Dieckmann (1952), the average total weight gain in eclamptic patients, compared to 22½ pounds in normal pregnancy.

It has long been known that the degree of water retention does not increase parallel to the severity of other manifestations of toxaemia (Browne, 1946). In some patients with considerable oedema, there may be little rise in blood pressure; on the other hand, in some of the worst cases of toxaemia, oedema, though present, is often not marked. Dieckmann acknowledges this clinical fact and concludes that "it appears to be the rate at which gains in weight occur, instead of the total amount of weight gain, which is of the first importance".

In the case of Mrs. G.M. the weight gain from the 32nd to the 34th week was only 4 ounces whereas she gained 4 pounds between the 34th and the 36th week. This preceded a sudden rise in her blood pressure. During the next 2 weeks she gained only 2 pounds 3 ounces. Thus the rate of increase after the 36th week gave less indication that this patient was developing toxaemia.

(b) *Blood Pressure*

The record of Table I shows little evidence of toxaemia apart from slight hypertension. At the time when she was suffering from eclampsia—before shock and post-partum haemorrhage may have lowered the readings—she had a blood pressure of 130/90. Once the diastolic pressure had risen to 90 it remained at that level until the onset of labour.

More significant than the absolute readings, however, is the marked relative increase in the patient's blood pressure between the 36th and 37th week above her average pressure. Although

it is true that in eclampsia the systolic pressure is usually well above 140, the patient had eclampsia when her systolic pressure was 130. The diastolic pressure which is perhaps less impressive, but more stable, would have been a more reliable guide in the diagnosis of toxaemia.

Many workers depend on the systolic pressure, and in a series reported by Cruickshank, Hewitt and Couper (1927) fewer than 20 per cent of their eclamptic patients had a systolic pressure of less than 141 mm. Hg. In Seitz's clinic (1951) 11·9 per cent (14 cases out of 117) of eclamptic patients had a blood pressure below 130.

(c) *Absence of Albuminuria*

No albuminuria was found throughout the patient's pregnancy, including the last urinalysis 13 hours before death. Post-mortem examination of the kidneys showed degenerative and necrotic changes, but it is difficult to decide how long before autopsy these changes had developed.

Eclampsia without albuminuria is generally considered to be uncommon, but in Olson's series (1953) of 48 cases of eclampsia, 7 patients had no albumen in their urine.

Usually, however, when albuminuria is absent there are other obvious signs of toxaemia.

(d) *Absence of Convulsions and Coma*

The occurrence of eclampsia without convulsions has been known for a long time. By 1933 King was able to collect 33 cases from the literature and add 1 of his own. Reis and Bernick (1944) brought the total number of reported cases up to 45. The incidence of non-convulsive eclampsia may well be much higher than the number of reported cases suggests. Way (1947), in his series of 33 fatal cases of eclampsia studied at autopsy, included 8 patients who had not had any convulsions. All patients had hypertension, except one, who was in a condition of shock at the time of admission. Amongst Jacobi's cases (1953) was one of hypertension and albuminuria treated by Caesarean section. Four days later, the patient gradually became comatose and died. Autopsy showed an eclamptic liver. Haller, Abels and Straus (1951) report a case of non-convulsive eclampsia where death was due to rupture of the liver caused by a haematoma bursting through the capsule: this cause of death has also been met with in eclampsia with convulsions (Weintraub, 1946).

That the liver can show the naked-eye appearance of eclampsia in the absence of any history of fits, was confirmed by Reinberger and Mackey (1951) in a patient who underwent Caesarean section for severe pre-eclampsia. During the operation the typical subcapsular haemorrhages were seen over the entire surface of the liver. The patient recovered.

In the case of Mrs. M. both convulsions and coma were absent. She was conscious, though drowsy, until shortly before she died. It is just conceivable that the absence of marked hypertension and oedema might account for the absence of convulsions. Eclampsia in which not only convulsions, but also coma, are absent, is very rare: Dieckmann and Wegner reported the 8th case in 1932. Had it not been for the characteristic changes in the liver, the case would have been regarded as one of pre-eclampsia.

The eclamptic patient of Reis and Bernick (1944) had no convulsions and questionable coma. There was only slight hypertension but a large amount of albumen was present in her urine 4 days before death. The liver showed the typical changes of eclampsia.

Are the pathological changes found in the liver of these patients in fact pathognomonic of eclampsia? Dieckmann (1948) observed several patients who showed no clinical evidence of eclampsia, yet the liver showed the characteristic lesions. He concluded that the periportal haemorrhages are not exclusive features of eclampsia. Sheehan (1950) considers that the liver changes are "found in nearly all patients who die of this condition" and occasionally "in patients who die suddenly at delivery without any previous indication of a toxaemia".

(e) *Circulatory Failure*

The patient's records (Table II) showed a persistently high pulse rate (130–160) and a moderate fall in blood pressure during the 5 hours following delivery. That the blood pressure was not as low as is usually observed in patients dying from shock, may have been due to underlying toxaemic hypertension.

The patient and her sister (whose case history is given below) presented the clinical features of shock. The apparent cause of the shock was blood loss in the first patient, and general anaesthesia and forceps delivery in the second. The autopsy findings in the first case revealed eclampsia and in the second case were suggestive of the same condition which, by itself, can cause circulatory failure. In severe toxaemia there is, according to Dieckmann (1952), a reduction in blood and plasma volumes. Any factors, such as operative delivery under general anaesthesia or post-partum haemorrhage may further decrease the blood volume and precipitate circulatory failure to which eclamptic patients are prone. The average patient does not die from a gradual post-partum haemorrhage of 2 pints, if the blood loss has been replaced by one of the plasma volume expanders. The striking clinical feature in the case of Mrs. M. was the failure to make a normal recovery in response to fluid replacement, as judged by pulse rate and blood pressure. Earlier transfusion with whole blood without crossmatching did not seem indicated at the time.

Mittelstrass (1947) acknowledged this failure of response to transfusion in eclampsia. He attempted to correlate the circulatory failure found in these cases with the condition of the cutaneous capillaries and retinal vessels. These showed dilatation of the capillary loops, particularly at the venous ends. The stasis in this type of circulatory failure results in haemorrhages and oedema. Transfusion with blood or blood substitute did not show any definite effect on the state of the capillaries.*

(f) *Family History of Eclampsia*

On enquiry into the family history of Mrs. M. it was found that one sister (Mrs. G.B.) was also aged 25 when she died from "non-convulsive eclampsia". A third sister (Miss D.S.), had died at the age of 26 from cardiac failure 7 hours after dental extraction under pentothal anaesthesia.

Case History of Mrs. G.B.

From the information available the following points appear relevant. The patient was seen at the antenatal clinic on 6 occasions. Her blood pressure and urine were normal until 4th August, 1942 (duration of pregnancy not known), when she was admitted to hospital with oedema, mild albuminuria and a blood pressure of 138/98. During the next 10 days the blood pressure and the amount of albumen in the urine remained the same. As there was no improvement the membranes were ruptured artificially 11 days after her admission. About 24 hours later, she had a low forceps delivery under light ether anaesthesia. The child, which was alive, was extracted without difficulty. The placenta was expressed manually.

Shortly after the patient came out of the anaesthetic, her pulse became feeble and her general condition deteriorated, although there had not been any excessive blood loss. It was thought that the primary cause of collapse was due to heart failure and cardiac stimulants were given without effect. Like her sister, she died 5 hours after delivery.

Only a summary of the necropsy findings was obtainable. This states that the liver showed "obvious patches of necrosis". In the kidneys "the glomeruli were small and many were necrotic. The epithelium of the collecting tubules showed degeneration to a marked degree."

As the full autopsy report was not available, Dr. A. M. Barrett, pathologist, was consulted. He agreed that the autopsy findings, taken in conjunction with the clinical picture, suggested that this patient, too, had died from eclampsia.

The case records of the two sisters have many curious points of resemblance, particularly the absence of convulsions. Mrs. G.B., however, had definite pre-eclamptic toxaemia. She was treated conservatively for 11 days and ultimately labour was induced.

It is not clear whether there is a hereditary tendency to eclampsia *per se*. Bickenbach (1939) found that 4 out of 39 eclamptics had knowledge of one or more cases of eclampsia in their families. There is probably, in some families, a predisposition to hypertension. The question whether this also applies to eclampsia in the absence of a family history of hypertensive disease is difficult to answer. Published family histories studied in this connexion showed a high incidence of vascular disease generally

* Schneider (1950) wonders whether some unexplained deaths in cases of toxaemia might be due to afibrinogenaemia. Dillon and Schmitz (1949) reported a case of fulminating eclampsia with fibrinogenopenia.

There were no grounds to suspect that this factor contributed to the deaths of the two sisters to which this paper refers.

(Theobald, 1933; Malpas, 1938; Dieckmann, 1952). Barnes and Browne (1945), in their survey, observed that eclampsia occurs also in families where there is no predisposition to hypertension.

Summary and Conclusions

(1) Details are given of a case of eclampsia without convulsions, coma, albuminuria, and with minimal hypertension.

(2) Reference is made to the patient's sister, who died at the same age, apparently also from eclampsia without convulsions.

(3) The absence of clinical signs of severe toxaemia is discussed and the importance of observing the diastolic blood pressure is emphasized.

One of the risks of being guided by a standard definition of hypertension (e.g., 140/90) is that patients with a normally low blood pressure may show a marked rise of pressure due to toxaemia, yet they may not reach the standard. This applies particularly to systolic readings.

(4) The diagnosis of eclampsia without convulsions is usually made at autopsy when the lesions, generally regarded as typical, are found in the liver. Had these patients not died, they might have been regarded as cases of pre-eclampsia. A series of observations on the appearance of the liver in patients treated by Caesarean section for pre-eclampsia may answer the question. Subcapsular haemorrhages can occur in the liver without the classical symptom of epigastric pain.

(5) As in some cases of eclampsia fibrinogen deficiency occurs, it may be advisable to avoid the use of polymerized glucose preparations. Blood, preferably fresh, should be given, in order to replace blood loss, and in some cases the time allowed for crossmatching may have to be reduced in order to forestall irreversible shock.

(6) In view of the tendency to circulatory failure as a cause of death in eclampsia, every care must be taken to avoid post-partum haemorrhage, as these patients tolerate it particularly badly.

(7) There does not seem to be any published evidence that non-convulsive eclampsia tends to run in families.

Acknowledgments

I am indebted to the late Dr. H. Middleton for the necropsy report on Mrs. G.M.; to Dr. A. M. Barrett for his opinion on the necropsy findings and for the histological report on the sections of the liver and kidneys of Mrs. G.M.; to Miss M. D. Power, of the Maternity Hospital, Sunderland, for supplying details of the case of Mrs. G.B.; and to Mr. Oswald Lloyd for permission to publish this paper.

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CHLORPROMAZINE IN THE TREATMENT OF ECLAMPSIA

BY

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EFFICIENT antenatal care has reduced to insignificance the incidence of eclampsia in many countries. In the less fortunate countries however eclampsia continues to be still a major problem and when it develops the well-established Stroganoff or modified Stroganoff therapy is usually resorted to. For obtaining the required sedation various drugs have been tried and, when response to conservative therapy has not been encouraging in some patients, Caesarean section or induction of labour in suitable cases to supplement the conservative treatment has been resorted to. These views and methods have been described in detail in previous publications (Menon, 1953, 1955).

In December, 1950, Chlorpromazine (Largactil) was synthesized by Charpentier in France during the course of a systematic study of Phenothiazine derivatives. In 1951, Laborit and Huguenard in Paris used it for the first time for their technique of "artificial hibernation". In January, 1952, Delay and Deniker used it in anaesthesia and in July, 1952 it was used in psychiatry. There have been few drugs in modern medicine to which so many properties have been ascribed. Amongst its important actions are: (*a*) its ability to lower body temperature—hypothermia, (*b*) potentiating action of other drugs, (*c*) hypotensive action and (*d*) narcosis. In 1953 Aoustin used it in the treatment of eclampsia for the first time. In France, Grasser and his colleagues reported its use in one case of eclampsia in 1953 while in the same year Baccaglini (Italy) reported another case. In November, 1953 Professor Schmidt-Elmendorff (in reply to Roettger's paper before the Rhine and Westphalian Society for Obstetrics and Gynaecology in Düsseldorf) gave his experience of the modified Stroganoff regime using Chlorpromazine, Diethazine and Phenobarbitone in the treatment of eclampsia. In July, 1955, Subodh Mitra (India) reported briefly his results in 46 eclamptics treated with Chlorpromazine and Promethazine. All these reports were encouraging and hence it was decided to treat a series of cases of eclampsia using these drugs.

A modified Stroganoff regime as given below was first tried in 28 cases.

1st day on admission:

0 hours	25 mg. of Chlorpromazine (Largactil) in 20 ml. of 5 per cent glucose is given intravenously and 50 mg. of Largactil plus 25 mg. of Promethazine (Phenergan) plus 0·2 g. of Phenobarbitone intramuscularly.
0+ 4 hours	25 mg. of Phenergan and 0·2 g. of Phenobarbitone intramuscularly.
0+ 8 hours	50 mg. of Largactil intramuscularly.
0+12 hours	25 mg. of Phenergan and 0·2 g. of Phenobarbitone intramuscularly.
0+16 hours	50 mg. of Largactil intramuscularly.
0+20 hours	25 mg. of Phenergan and 0·2 g. of Phenobarbitone intramuscularly.
0+24 hours	50 mg. of Largactil intramuscularly.

The same schedule is followed the next day also. Not more than 1,000 ml. of 20 per cent glucose solution is given intravenously on the

first and second days. An indwelling catheter is kept in the bladder and the urinary output recorded every hour. The temperature, pulse, respiration and blood pressure also are recorded hourly. In all ante-partum eclamptics if the fits are not controlled by this regime within a reasonable time (8–10 hours) pregnancy is terminated either by Caesarean section in those patients with unripe cervices and unengaged heads or by artificial rupture of membranes in those with ripe cervices indicating quick response to induction. In the intra-partum eclamptic labour is accelerated by artificial rupture of membranes and the second stage in all cases is cut short by outlet forceps if necessary. The post-partum eclamptic is treated by sedation as above.

Twenty-eight cases were treated on these lines. Seventy-five per cent of the patients were primigravidae. Ten per cent were at term, 70 per cent were between 34- and 36-weeks pregnant, 15 per cent 32 to 34 weeks, and 5 per cent between 28 and 32 weeks. In this series there were 14 ante-partum, 6 intra-partum and 8 post-partum eclamptics. According to the London Committee's classification, 18 were severe eclamptics and 10 mild ones. Some of the important relevant details are given below in Table I.

Of the 20 ante- and intra-partum cases, one was delivered by Caesarean section—indications being repeated convulsions (34) in spite of sedation for 10 hours in a primigravida with unengaged head and unripe cervix. After the section she did not have a single convulsion and made an uneventful recovery. The baby, weighing 5 pounds, was discharged in good condition along with the mother on the eighteenth day. In 10 cases the membranes were ruptured artificially. Six patients delivered by outlet forceps. In this series, the incidence of recurrence of fits was 38 per cent in the severe eclamptic and 15 per cent in the mild. Two mothers died; both had ante-partum eclampsia.

From the point of view of control of convulsions and reduction of maternal mortality in the severe eclamptic I conclude that this method was not good enough. But during the course of treatment I was struck by the following factors:

(*a*) The absence of pulmonary complications.

(*b*) The absence of hyperpyrexia.

(*c*) The effect on blood pressure.

(*d*) The general satisfactory appearance of the patient.

(*e*) The good urinary output.

If I could obtain more sedation I thought it might give me better results and hence the treatment was modified as follows.

The Promethazine was replaced by another Phenothiazine derivative namely Diethazine (Diparkol). Its pharmacological properties comprise: (*a*) an ability to depress the excitability of the autonomous nervous system with action on both the sympathetic and parasympathetic outflow, (*b*) a central analgesic action, (*c*) a temperature lowering action, (*d*) a slight antihistamine action, and (*e*) a slight spasmolytic action. The Phenobarbitone was replaced by

TABLE I

Type	A.P. and I.P.	P.P.	Blood Pressure Highest	Blood Pressure Lowest	Blood Pressure Average	Average No. of Fits Before Treatment	Percentage of Recurrence of Fits	Urinary Output Good	Urinary Output Poor	Results Mother	Results Child
Severe ..	13	5	220 / 130	150 / 100	190 / 120	13·6	38	17	1	2D	5 SB 1 ND
Mild ..	7	3	160 / 110	130 / 100	150 / 110	4·4	15	10	—	Nil	1 SB

Pethidine. The modified treatment is given below:

On admission:

0 hours — 25 mg. of Largactil and 100 mg. of Pethidine in 20 ml. of 5 per cent glucose are given intravenously.
50 mg. of Largactil and 50 mg. of Diparkol intramuscularly.

A drip of 20 per cent Dextrose solution containing 200 mg. of Pethidine is then set up and this is run in slowly at 20 to 30 drops a minute, the rate depending upon the response to treatment. If the patient is quiet the rate of the drip is reduced; if restless it is increased till she is quiet. Not more than 1,000 ml. of 20 per cent Dextrose is given in 24 hours and in all not more than 300 mg. of Pethidine in the 24 hours.

0+ 4 hours — Diparkol 50 mg. intramuscularly.
0+ 8 hours — Largactil 50 mg. intramuscularly.
0+12 hours — Diparkol 50 mg. intramuscularly.
0+16 hours — Largactil 50 mg. intramuscularly.
0+20 hours — Diparkol 50 mg. intramuscularly.
0+24 hours — Largactil 50 mg. intramuscularly.

The same schedule of treatment without Pethidine is continued the next day also, Largactil and Diparkol being given alternately intramuscularly in 50 mg. doses every 4 hours. If the fits are not controlled within 8 to 10 hours either Caesarean section or artificial rupture of membranes is done in those who are not in labour depending upon the nature of the cervix.

Fifty cases were treated on these lines. Seventy per cent of the patients were primigravidae. Ten per cent were at term, 72 per cent were 34- to 36-weeks pregnant, 10 per cent between 32 and 34 weeks and 8 per cent between 26 and 32 weeks. Thirty were ante-partum eclamptics of whom 20 were severe types. Among the 10 intra-partum eclamptics 6 were of the severe type and in the 10 post-partum eclamptics there were 6 severe cases. Some of the relevant important details are given below in Table II.

The recurrence of fits among the 32 severe eclamptics was reduced to 10·2 per cent and in the mild cases it was nil. Two patients among the 20 severe cases of ante-partum eclamptics were delivered by Caesarean section, the indication being failure to control convulsions despite 10 hours of treatment. Each of these patients had 26 and 32 fits respectively and not a single convulsion after the section. They had an uneventful recovery and left the hospital with live babies. In 12 patients the membranes were ruptured artificially. Vaginal delivery by outlet forceps was resorted to on 18 occasions in the 40 ante- and intra-partum eclamptics. Only one mother was lost—a severe ante-partum eclamptic. The incidence of stillbirths and neonatal deaths among the 40 ante- and intra-partum eclamptics was 25 per cent.

Some Observations

Blood Pressure. Of the 78 cases treated by Chlorpromazine 70 per cent of cases showed significant drop in blood pressure during therapy and before delivery. In 25 per cent no significant drop in blood pressure was noted. In 5 per cent there was an elevation of the blood pressure.

Table II

Type	A.P. and I.P.	P.P.	Blood Pressure Highest	Blood Pressure Lowest	Blood Pressure Average	Average No. of Fits Before Treatment	Percentage of Recurrence of Fits	Urinary Output Good	Urinary Output Poor	Results Mother	Results Child
Severe ..	26	6	230 / 140	150 / 110	180 / 130	14·3	10·2	29	3	1D	6 SB 2 ND
Mild ..	14	4	170 / 120	140 / 90	150 / 95	5·6	Nil	18	—	—	1 SB 1 ND

The maximum drop obtained was 60 mm. Hg systolic and 40 mm. Hg diastolic in a patient with a pressure of 210/130. The average drop was 30 mm. Hg systolic and 15 mm. Hg diastolic. The drop was maintained for less than 2 hours in 70 per cent of the cases, in 20 per cent for 6 hours, in 6 per cent for 8 hours and in 4 per cent the pressure did not rise after the initial drop. It was observed that the range of fall in systolic pressure was more marked than the diastolic. Post-partum eclamptics showed a more consistent and larger range of drop than the ante- and intra-partum cases. In 2 cases during the course of the treatment the blood pressure fell to 90 mm. Hg systolic but no bad effects followed. No further drop in pressure occurred even though the treatment was continued. It may be mentioned here that during trials with Apresoline in the management of pre-eclamptic toxaemia it has been found that addition of 25 mg. of Largactil to the injected Apresoline not only enhances the range of fall of blood pressure but also prolongs the duration of the drop. The inference is that Chlorpromazine is a useful hypotensive drug which can be used safely in the acute stage of the disease though its action is not always certain and varies in different individuals.

The Pulse: Tachycardia was noticed in all cases and this was evident within an hour of the start of the treatment. On an average the pulse rate increased by 16 beats per minute. No untoward effects were noticed.

Pulmonary Complications. In my previous study of 174 deaths among 1,150 eclamptics, pulmonary complications were present in 40 per cent of cases and 29·5 per cent of the fatal cases showed evidence of pulmonary oedema. It is remarkable that in this series of 78 cases not one patient developed pulmonary oedema and only 2 cases showed evidence of pulmonary congestion. The respirations during treatment were easy and quite normal in rate. At no time was cyanosis observed and oxygen was given only on one occasion. Secretions from the upper respiratory tract were conspicuous by their absence and the necessity for the frequent clearing of the throat for keeping the airway open seldom arose. This in my opinion is a very major advantage.

The Urinary Output. Maintenance of a good urinary output is essential in eclampsia. During this treatment in 95 per cent of the cases the urinary output was good. In 3 cases it was diminished and only in 1 case did it give rise to anxiety. However the output came to normal soon after delivery. On an average even the severe eclamptic passed 780 ml. of urine per day during treatment.

Temperature. Among the fatal eclamptics in my previous analysis referred to, hyperpyrexia as a terminal event was present in 25·3 per cent of cases. In this group, no patient had hyperpyrexia and only 3 patients had a temperature of 103° F. Hyperpyrexia in an eclamptic is a dreaded event and it was conspicuous by its absence in this series. I believe it could be attributed to the hypothermic property of Chlorpromazine.

The Control of Fits. Using Chlorpromazine along with Phenergan and Phenobarbitone the percentage of recurrence of fits was high. When Phenergan and Phenobarbitone were replaced by Diethazine and Pethidine the incidence of recurrence fell to 10·2 per cent which compares not unfavourably with the recurrence rate when other sedatives are used—Thiopentone, 9·5 per cent (Menon, 1953), Bromethol, 6·8 per cent (Dewar and Morris, 1947). Considering that 32 out of the 50 were severe eclamptics and that all of them were emergency admissions who had no antenatal care worth mentioning the effectiveness to control the convulsions should be stated to be good.

Chlorpromazine is said to have an anti-shock property also. The absence of shock in the Caesarean sections done under local anaesthesia and in other operative deliveries in this series was another noteworthy feature. The post-operative convalescence of the Caesarean section patients was strikingly smooth.

Equally striking has been the absence of post-eclamptic psychosis among this series. Post-eclamptic psychosis is a well recognized clinical complication of the puerperium which can be very distressing and sometimes even fatal. In this series only 2 patients developed mild psychosis and they responded easily to Chlorpromazine.

I conclude that the combination of Chlorpromazine, Diethazine and Pethidine constitutes

a form of conservative therapy which is reasonably effective in the control of convulsions. It has also the added advantage that pulmonary complications, hyperpyrexia and shock which enhance the death rate are reduced to the minimum and hence helps to reduce the maternal death rate. However, I believe that if within a reasonable time the convulsions cannot be controlled by this treatment, Caesarean section or artificial rupture of the membranes could supplement with advantage the conservative regime as mentioned in a previous publication (Menon, 1955). Three Caesarean sections were done in this series with very good results.

Summary and Conclusions

(1) A preliminary report on 78 cases of eclampsia treated by Chlorpromazine in combination with Promethazine and Phenobarbitone (28 cases) and in combination with Diethazine and Pethidine (50 cases) is presented.

(2) The combination of Chlorpromazine, Promethazine and Phenobarbitone was not satisfactory in the sense that the incidence of recurrence of fits in the severe cases was 38 per cent and the maternal mortality 7·2 per cent.

(3) Better results were obtained when Chlorpromazine was combined with Diethazine and Pethidine. In the mild cases the incidence of recurrence of fits was nil and in the severe cases only 10·2 per cent.

(4) The impressive features observed during treatment were the absence of pulmonary complications, hyperpyrexia, shock and post-eclamptic psychosis and the good urinary output.

(5) Out of 50 cases treated by this combination only one mother was lost. Two patients were delivered by Caesarean section due to the fits not being controlled. The foetal mortality for the whole series was 25 per cent.

It is a pleasure to express my thanks to the medical officers and nursing staff of the hospital who spared no pains in the management of these cases and in keeping detailed notes.

I am deeply indebted to Messrs. May & Baker who provided us with generous amounts of Largactil, Diparkol and Phenergan for the clinical trial.

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TUBAL PLASTIC OPERATIONS*

BY

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ALMOST since the advent of modern gynaecological surgery attempts have been made to preserve diseased Fallopian tubes and to repair those blocked by infection or congenital malformations. Perhaps the first such effort was made by Schröder (1884), who opened and repaired the pus-filled tubes of a 21-year-old nulligravida in 1881. That she recovered from the operation may be taken for granted, although no mention is made of subsequent pregnancies. Present on this occasion was Schröder's colleague, A. Martin (1891), who was able to present 21 such cases to the Gesellschaft für Geburtshilfe und Gynäkologie in Berlin in July 1884. Again there were no term pregnancies reported although one abortion did occur in the series.

Stimulated by the German work Polk (1891), McMonagle (1894) and Burrage (1900) in America all published on conservative, partially reparative operations on the Fallopian tubes. This widespread attempt at conservatism is well covered in the early editions of Kelly's *Operative Gynecology* (1912). Sporadic pregnancies certainly occurred, although from the reports available it is difficult to tell how often the patient possessed at least one patent tube. Burrage summed up the situation succinctly with the statement: "With the present methods of resecting tubes, if both are closed, pregnancy is not to be expected." These operations were undoubtedly performed on chronically ill patients with salpingitis and frequently with peritonitis. The fimbriated ends only were opened and repaired. The conservative handling of the adnexa followed sound gynaecological tradition, and pregnancy, if any, came as a delightful but quite unexpected sequel.

Similarly, blockage at the cornu was attacked conservatively. T. J. Watkins, operating for a cornual myoma in a patient whose opposite tube and ovary previously had been removed, resected the tumour and implanted the remaining portion of the tube (Ries, 1897). A pregnancy followed that ended in an abortion. Shaw (1921) reports a subsequent case operated on by T. J. Cullen. The patient had a previous unilateral salpingo-oöphorectomy. An interstitial pregnancy was resected and the remaining tube implanted in the cornu. As in the former case a pregnancy followed but terminated in a 7-months stillbirth complicated by a placenta praevia.

Attempts to restore fertility after salpingectomy by means of implanting the pedicle of the ovary into the uterine cavity through a posterior fundal incision were first made by Tuffier of Paris (1924). This operation has been abandoned and largely supplanted by types of cornual implantation first suggested by Estes (1924). The success rate of these procedures is probably less than 4 per cent.

Although these developments were followed by a host of reports of conservative management of Fallopian tubes and ovaries at operation, none of the procedures were directed primarily at the cure of sterility. Planned operative procedures to correct anatomic defects came only with the advent of modern methods for the diagnosis of tubal occlusion. Foremost among these methods are Rubin's test (1920) and the development of X-ray visualization of the tubes (Cary, 1914). Another advance was the introduction of the culdoscope by Decker and Cherry in 1944.

* Green-Armytage Anglo-American Sterility Lecture delivered at the Royal College of Obstetricians and Gynaecologists, 25th May, 1956.

In the meantime, numerous case and a few series reports appeared, some favourable and others not. Solomons (1936) instituted the general type of questionnaire survey and this was followed by Greenhill's (1937) most discouraging analysis one year later. From 107 leading American gynaecologists the latter investigator was able to collect 818 tubal plastic operations with a 6·6 per cent pregnancy rate and 4·4 per cent live babies. The accompanying comments were pessimistic indeed. Greenhill's report had a devastating effect in America and tubal plastic surgery fell into disrepute. However, abroad and particularly in England under the inspiration of Victor Bonney (Berkeley and Bonney, 1947), these operations continued to be done.

Stimulated and encouraged by Dr. John Rock of Boston, the author undertook a small series of such operations, employing more delicate techniques than had hitherto been described and making use of a polyethylene prosthesis. A preliminary report (Hellman, 1951) was somewhat encouraging. Although there was only 1 pregnancy in 8 cases in which the tubes were reconstructed over polyethylene, all but one of the tubes remained open after the operation. This paper and the subsequent encouraging results of Rock, Mulligan and Easterday (1954), Green-Armytage (1952) and others stimulated a rebirth of operative enthusiasm.

The paper this afternoon will first report the result of an attempted world-wide survey of tubal plastic procedures by Dr. Alvin Siegler and the author (1956) and secondly will briefly describe the author's personal results along with certain minor operative tricks gleaned from nearly ten years of trial and error.

The survey was made under the auspices of the American Society for the Study of Sterility with the hope that the results would show improvement over those cited by Greenhill nearly 20 years before. This hope was based on the advent of better diagnostic and operative techniques, transfusion, chemotherapy and antibiotics.

The questionnaire was sent to 4,900 physicians in 3 groups:

(1) All diplomates of the American Board of Obstetrics and Gynecology.

(2) All members of the American Society for the Study of Sterility not in Group 1.

(3) Physicians residing outside the United States who were known to be interested in female infertility.

The results of this study have just been published and are merely reproduced here in brief summary.

Only 734 of the 4,900 physicians answered the questionnaire. The fact that there was only a 15 per cent response is the most serious defect of the study and makes unstable any conclusions drawn (Table I). Furthermore, only

TABLE I
Response to Questionnaire

Country	No. Sent	No. Replies	Per cent Response
U.S.A.	3,750	651	17·4
Canada	360	8	2·3
Foreign	800	75	9·3
Total	4,910	734	15·0

84 men or 11 per cent of those responding could be considered to be "experienced" in this field by having done 10 or more operations (Table II).

TABLE II
Tubal Plastic Experience

Response	Number	Per cent
No. Surgery	365	50·0
Less than ten cases ..	285	39·0
Ten cases or more	84	11·0

In other words, less than 2 per cent of those queried reported any significant experience along these lines. These surgeons did a total of 2,285 operations and it was this group of procedures that was analyzed in detail. The number of operations is large and if it had been representative of the activity in this field it could have been meaningful. However, there is evidence to suggest that many surgeons most active in this particular aspect of sterility strongly disapproved of the questionnaire method and did not submit their data.

The results for salpingolysis are shown in Table III. Nine hundred and thirty-one operations resulted in 270 pregnancies, 78 per cent of

TABLE III
Salpingolysis

Surgeons	Operations	Outcome of Pregnancy				Total Pregnancies
		Ectopic	Abortion	Stillbirth	Live Birth	
68	931	20 (7·3 per cent)	38 (14·2 per cent)	0	212 (78·5 per cent)	270 (29 per cent)

which were live births, a pregnancy rate of 29 per cent and "absolute success" rate of 22·6 per cent.

There were 891 instances of salpingostomy fimbriae, resulting in 134 live births and having a total pregnancy rate of 20·6 per cent (Table IV). Similarly, there were 272 tubal implantations and 191 resections with 24 and 8 live births respectively and pregnancy rates of 16·1 and 7·8 per cent (Tables V and VI).

Table VII presents a summary of the material. Out of a total of 2,285 tubal plastic operations there were 378 live births or a rate of 16·5 per cent. The total pregnancy rate was 22·5 per cent with 26·3 per cent of the pregnancies being lost in either ectopic implantations, abortions or stillbirths. Excluding salpingolysis the liveborn pregnancy rate was 12·3 per cent.

These results are some three times better than those obtained by Greenhill, but should be viewed with caution for the reasons explained above. It is extremely doubtful whether any questionnaire method can give reliable results in this field. In the first place, it is difficult to categorize operative procedures as has been done in the above study, for very frequently more than one operation and more than one type of operation is done on the same patient.

TABLE IV
Salpingostomy

Surgeons	Operations	Outcome of Pregnancy				Total Pregnancies
		Ectopic	Abortion	Stillbirth	Live Birth	
72	891	22 (12·0 per cent)	21 (11·8 per cent)	7 (3·7 per cent)	134 (72·5 per cent)	184 (20·6 per cent)

TABLE V
Tubal Resection

Surgeons	Operations	Outcome of Pregnancy				Total Pregnancies
		Ectopic	Abortion	Stillbirth	Live Birth	
53	191	1 (6·6 per cent)	5 (33·0 per cent)	1 (6·6 per cent)	8 (53·8 per cent)	15 (7·9 per cent)

TABLE VI
Tubal Implantation

Surgeons	Operations	Outcome of Pregnancy				Total Pregnancies
		Ectopic	Abortion	Stillbirth	Live Birth	
51	272	4 (9·2 per cent)	15 (34·0 per cent)	1 (2·3 per cent)	24 (54·5 per cent)	44 (16·1 per cent)

TABLE VII
Summary of 2,285 Tubal Plastic Operations by 84 Surgeons

Type	Operations	Total Pregnancies		Pregnancy Wastage		Live Births	
		No.	Per cent	No.	Per cent*	No.	Per cent†
Salpingolysis	931	270	29·0	58	21·5	212	22·8
Salpingostomy	891	184	20·6	50	27·2	134	15·0
Tubal implantation	272	44	16·1	20	45·1	24	8·8
Tubal resection	191	15	7·8	7	46·5	8	4·2
Total	2,285	513	22·5	135	26·3	378	16·5

* Per cent of total pregnancies.
† Per cent of operations.

Secondly, it may be that the aetiology of the tubal blockage is of more important prognostic significance than the type of operation performed and, finally, the response to the questionnaire is largely from those opposed to the operation, or those with very good results. Perhaps the best indication that these operations are of value is that the patients, fully informed about the available figures, continue to seek surgical cure, and competent surgeons continue to experiment and explore the operative cure of tubal occlusion.

The successful performance of reparative operations on the Fallopian tubes requires meticulous attention to certain details. Only the most gentle and finished techniques can hope to yield a high percentage of tubal patency. These appendages cannot be roughly handled. The squeezing of the tubes between the fingers is enough to produce leukocytosis and oedema. The instruments used should be the most delicate. Those designed for eye operations are preferable and the suture material must also be extremely fine; 00000 silk or catgut with atraumatic needles or small French needles are all that should be used. The dissection should always be sharp and the field should be scrupulously dry and bloodless. The tubes should be manipulated either with very fine forceps or silk guide sutures. Figure 1 shows the method currently used to obtain an almost completely dry field. This is of particular advantage if the uterus is to be opened. More and more we have resorted to this latter procedure for it makes manipulation of the polyethylene prosthesis easier and simpler. Furthermore, the catheters can be anchored both to the skin and as in the insert in Figure 2, or through the cervix or both. The small rubber-shod bulldog clamps are applied to the ovarian vessels on both sides and to the uterine vessels through a perforation in the clear area of the broad ligament. The uterine vessels are not usually dissected free as in the diagram but nevertheless can be clamped quite satisfactorily from this position. The vessels are not injured in any way by these clamps. Even in operations for occluded fimbriae, if polyethylene is to be used, it may be well to open the fundus as shown in Figure 2. In these cases we perform the usual operation of removing part of the club-shaped end of the tube with a diagonal cut and then suturing the mucosa to the serosa with a fine over and over catgut suture. A soft silver probe with a slightly bulbous end as shown in Figure 2 or a number 4 nylon ureteral catheter as in Figure 3 is passed either down or up the Fallopian tube. The choice depends on whichever is easier and less traumatic. If the probe is used the catheter may be threaded over the end as in Figure 1. Usually it will stick fast but if its lumen is slightly large it may be made smaller by stretching the catheter as in insert A, Figure 4. If the nylon catheter technique is employed, and sometimes this passes through the interstitial portion of the tube far more easily than the probe, then the polyethylene tube may be simply passed over the end of the stylet and tied with a silk tie as shown in Figure 4, insert B, or the polyethylene prosthesis may be threaded over the catheter as shown in insert B, Figure 4. Once the polyethylene prosthesis has been threaded over the

probe or over the stylet of the catheter or over the catheter itself, it can easily be drawn through the tube. This is one of the most difficult and perplexing aspects of the operation but with these manœuvres the prosthesis usually can be passed through the tube without serious trauma. The polyethylene catheter can then be passed through the cervix either by means of a Weisman hollow brass tube (Fig. 4) or by means of a simple probe to which it has been tied. Both are pulled through the cervix from below. The anastomoses are done either at the cornu or in the isthmus with fine interrupted submucosa to submucosa catgut sutures and reinforced with interrupted silk serosal sutures. It has been our practice to bring the polyethylene catheter through the skin lateral to the midline incision by threading it through a large sharp needle. It is then anchored to the skin between two crushed lead beads by means of a silk suture. The end that protrudes from the cervix is also closed with a crushed lead bead and can be anchored or not as the operator desires.

In the absence of Fallopian tubes we have tried somewhat unsuccessfully to create permanent uterine fistulas using slightly larger polyethylene as in Figure 5.

This afternoon I wish to present to you the results of 36 operations for bilateral tubal occlusion performed on 34 patients since 1948. No patients having salpingolyses alone are included, for this particular operation yields results of a different order of magnitude than those with true tubal blockage.

No patient in this series was submitted to operation unless repeated tests had shown conclusively that the Fallopian tubes were blocked bilaterally. In some cases this was demonstrated by repeated tubal insufflation, but in most instances salpingograms were taken and in many culdoscopy was performed. Obviously those patients whose Fallopian tubes were absent and those with previous sterilization did not require such tests.

The cases have been divided into four groups according to the known or suspected aetiology of the sterility. To some extent, but not always, this indicated the type of operation. There were 3 patients who had had tubal ligation and two with previous bilateral salpingectomy. There were 5 operations for nodular enlargement of the tubes at the cornua. Although the microscopic picture of salpingitis isthmica nodosa, namely, increased muscle and connective tissue and many diverticula of the tubal lumens, could not be demonstrated in all of these, it was present in the majority and in the others the gross picture was so typical as to be almost conclusive. The exact aetiology of this condition is unknown (Shenkin and Burns, 1943); however, none of these patients gave the least indication of any previous infection. There were 23 operations on patients with a history of infection. Seven of these were service patients from the Kings County Hospital, where the incidence of gonorrhoeal infection is high.

The 3 patients who had been sterilized (Table VIII) all apparently had had Pomeroy ligations. The sealed ends of the tubes lay about 2 centimetres apart in the abdomen and there were no adhesions. The blunt ends of the tubes were cut off and polyethylene catheters threaded through the distal portions and into the proximal ends. The uteri in these cases were not opened. An end to end anastomosis was done as previously indicated and the prothesis brought out through the skin. Post-operative Rubin's test was not done in one, negative in one, not done

TABLE VIII
Attempted Correction of Infertility Due to Tubal Ligation

Name	Age	Diagnostic Procedures			Operation	Prosthesis	Results	
		Rubins	Salpingography	Culdoscopy			Rubins	Pregnancy
A.P. ..	—	0	0	0	Anastomosis	Polyethylene	0	0
L.D. ..	30	0	0	0	Anastomosis	Polyethylene	N.D.	4 term
A.F. ..	29	0	0	0	Anastomosis	Polyethylene	Unknown	0

FIG. 1

Occlusion of the uterine circulation with rubber-shod curved bulldog clamps on the ovarian and uterine vessels.

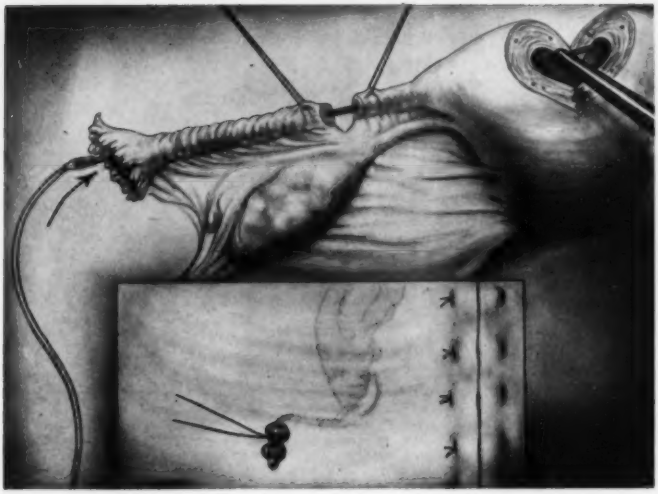

FIG. 2

Threading of a polyethylene catheter on a silver probe through a resected Fallopian tube into the exposed endometrial cavity. Insert shows a method of fastening the free end of the catheter to the skin.

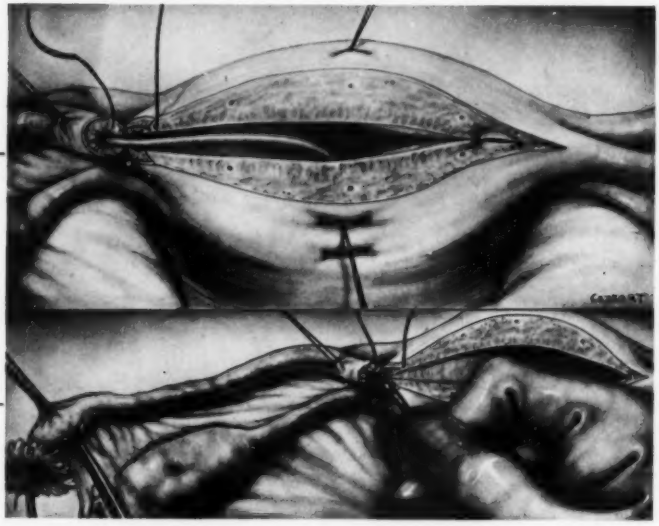

FIG. 3

B: Threading a No. 4 nylon ureteral catheter through the Fallopian tube following a corneal resection.

A: The nylon catheter has been followed by one of polyethylene. This is passed through the cervix. The first suture of the uterotubal anastomosis is in place and the fundal closing sutures have been started.

L.M.H.

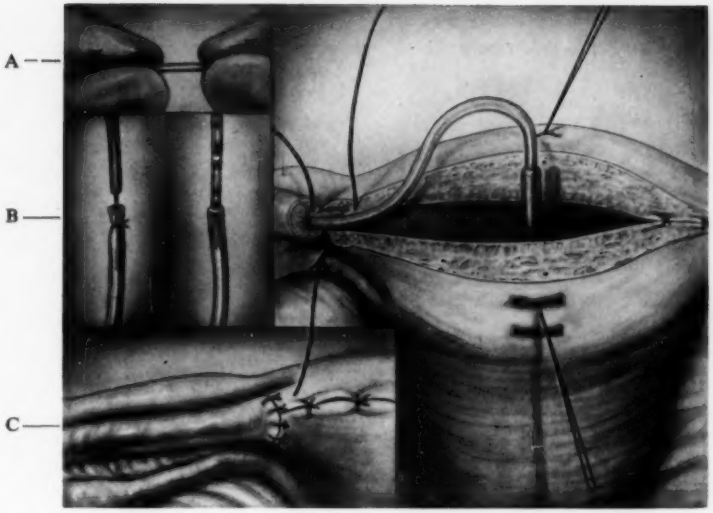

FIG. 4

A polyethylene catheter being passed through cervix with a Weisman introducer.
A: Method of reducing lumen of a polyethylene catheter.
B: Method of following nylon catheter by polyethylene catheter.
C: Final closure of corneal resection.

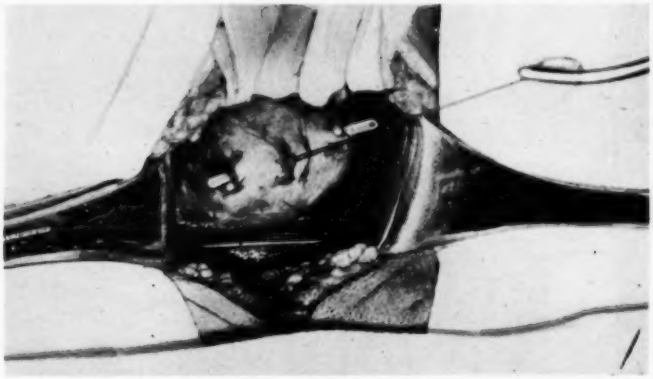

FIG. 5

Method of creating permanent uterine fistulas in cases with previous bilateral salpingectomy.

in another because of a supervening pregnancy. The last patient has now had 4 term living children since the operation.

In the patients with previous salpingectomy, a hysterostomy was performed. The ostia were made with a sharpened cork-borer, a core of tissue being thus removed. Number 260, OD. 11 inches, polyethylene catheters were inserted and passed through the cervix. They were held in place with fine catgut sutures placed through the wall of the catheters. The prostheses were allowed to remain in place for 2 weeks. The results as indicated in Table IX were disappointing in that the fistulas did not remain open.

In Table X are shown the 5 patients with salpingitis isthmica nodosa. The cornua were resected. In 3, holes were made in the cornua and the tube, threaded over a polyethylene catheter, was sutured in place according to the techniques developed by Holden and Sovak (1932), Green-Armytage (1954) and others. In the last 2 the fundus was opened as illustrated in the previous figures. In one no follow-up test for patency was done. In 1 the tubes were occluded and in 3 the Rubin's test was positive. There have been no pregnancies to date.

In the 19 private operations listed under the heading "Infection" (Table XI) 6 followed appendicitis, 2 were postabortal. One patient, operated on twice, had mild tuberculous salpingitis and the remainder are presumed to be gonorrhoeal. The majority of the operations were fimbriaplasties as previously described. Most had polyethylene prostheses. Two of the patients were operated on twice. In both instances the second operation was performed to retrieve a catheter which had broken off at the skin margin and had been retracted into the peritoneal cavity. In one of these vinethyl plastic had been used. This is brittle and probably not suitable for these procedures. In both cases the tubes were found and reclosed and although another plastic procedure was carried out the results were unsatisfactory.

In the 7 patients from the service at the Kings County Hospital (Table XII) the tubal occlusion was considered to have been gonorrhoeal in origin. The post-operative tubal patency in these two series was 47·0 and 71·5 per cent respectively. There were 2 term living pregnancies in the private group and 1 in the service group.

Table XIII presents a summary of the entire series of 36 operations. There were 3 operative

TABLE IX
Attempted Correction of Infertility Due to Bilateral Salpingectomy

Name	Age	Diagnostic Procedures			Operation	Prosthesis	Results	
		Rubins	Salpingography	Culdoscopy			Rubins	Pregnancy
S.P. ..	34	0	0	0	Hysterostomy	Polyethylene	0	0
V.K. ..	25	0	0	0	Hysterostomy	Polyethylene	0	0

TABLE X
Attempted Correction of Infertility Due to Salpingitis Isthmica Nodosa

Name	Age	Diagnostic Procedures			Operation	Prosthesis	Results	
		Rubins	Salpingography	Culdoscopy			Rubins	Fertility
F.S. ..	38	+		+	Cornual resection	Polyethylene	+	0
H.S. ..		+	+	0	Cornual resection	Polyethylene	+	0
R.E. ..	33	+	+	0	Cornual resection	Polyethylene	0	0
L.D. ..	31	+	+	0	Cornual resection	Polyethylene	N.D.	0
H.R. ..	35	+	+	0	Cornual resection	Polyethylene	+	0

TABLE XI
Attempted Correction of Infertility Due to Tubal Infection

Name	Age	Diagnostic Procedures			Operation	Prosthesis	Results	
		Rubins	Salpingo-graphy	Culdo-scopy			Rubins	Pregnancy
F.A. ..	35	+	+	+	Bil. salpingostomy	Stainless steel	0	0
G.W. ..	25	+		attempted	R. salpingo-oöphorectomy L. salpingostomy	Polyethylene	0	0
H.S. ..		+		+	R. anastomosis and L. fimbriaplasty	Polyethylene	+	0
A.C.* ..	34	+	+	+	Bil. salpingostomy	Polyethylene	0	0
L.D.* ..	30	+		+	L. fimbriaplasty and R. release of adhesions	None	+	1 term
A.N.*		+			Pre-sacral neurectomy L. anastomosis	Polyethylene	0	0
M.D. ..	33	+		+	Bil. fimbriaplasty	Polyethylene	+	0
R.M.*	35	+	+		L. anastomosis	Polyethylene	0	0
S.D.* ..	24	+	+		Bil. fimbriaplasty	Polyethylene	N.D.	1 term
E.D.† ..	31	+	+		Bil. fimbriaplasty	Polyethylene	0	0
C.D.‡	26	+	+		Bil. fimbriaplasty Pre-sacral neurectomy	Vinethyl	0	0
A.B. ..	30	+	+		Bil. fimbriaplasty	Polyethylene	+	0
E.D.† ..	31	second operation			R. fimbriaplasty	Polyethylene	0	0
C.D.‡	27	second operation			Bil. fimbriaplasty	Polyethylene	0	0
E.W. ..	32	+	+		Bil. fimbriaplasty	Polyethylene	N.D.	0
E.T.* ..	36	+	+		L. fimbriaplasty	Polyethylene	N.D.	0
R.N. ..	31	+	+		Bil. fimbriaplasty and Bil. cornual excision	Polyethylene	+	0
L.S. ..	36	+	+		Bil. fimbriaplasty	Polyethylene	+	0
E.H. ..	36	+	+		L. fimbriaplasty and R. release of adhesions	Polyethylene	+	0

* Post appendicitis.
† Post abortal.
‡ Tuberculosis.

TABLE XII
Attempted Correction of Infertility Due to Tubal Infection
*Service Patients Kings County Hospital**

Name	Age	Diagnostic Procedures			Operation	Results	
		Rubins	Salpingo-graphy	Culdoscopy		Rubins	Pregnancy
S.H. ..	30	+	+	+	L. anastomosis and R. re-implantation		1 term
E.M. ..	33	+	+	+	Bil. fimbriaplasty	0	0
N.J. ..	23	+	+	+	Bil. fimbriaplasty	0	0
L.S. ..	26	+	+		L. fimbriaplasty R. fimbriaplasty and anastomosis	+	0
D.C. ..	28	+	+	+	Bil. fimbriaplasty	+	0
E.G. ..	27	+	+	+	Bil. fimbriaplasty and anastomosis	+	0
G.D. ..	23	+	+	+	Bil. fimbriaplasty	+	0
Total 7							1

* Courtesy Dr. Paul Topkins.

TABLE XIII
Summary of Tubal Plastic Operations, 1948–1955

Aetiology	Number	Complications	Per cent	
			Rubins Positive	Pregnancies
Tubal ligation	3	0	33·3	33·3
Salpingectomy	2	0	0·0	0·0
Isthmica nodosa	5	1	75·0	0·0
Infection	19	2	47·0	11·1
Infection*	7	0	71·5	14·3
Total	36	3	54·8	11·1

* Service patients courtesy Dr. Paul Topkins.

complications. Two have already been mentioned, namely, the loss of the catheters into the peritoneal cavity. The third was in a case of salpingitis isthmica nodosa. This patient had been given 200 milligrams of cortisone a day for 5 days prior to the operation in hope that the healing of the tubes would be delayed and fewer adhesions would form. She developed a post-operative cough and now has an incisional hernia. Whether this complication is related to the cortisone therapy cannot be determined.

In summary, certain modifications of the standard techniques for tuboplasty have been presented. These include methods of handling a polyethylene prosthesis with less trauma and more simply than hitherto practised.

An attempt has been made to determine the world status of these operations. Because of the shortcomings of the questionnaire method, the results of this survey can only be taken as suggestive. It would appear that less than 2 per cent of gynaecologists perform any number of these operations and that the liveborn rate following such operations, exclusive of salpingolysis, is approximately 12 per cent. The pregnancy wastage is 32 per cent.

Following the 36 operations presented the tubal patency rate was 54·8 per cent and the liveborn pregnancy rate was 11·1 per cent. Interestingly, there was no pregnancy wastage in this series.

These rates are nowhere near so high as those reported by Green-Armytage (1955) or Rutherford, Lamborn and Banks (1949), nor are they quite so good as the last series reported by Rock and his colleagues (1954). Nevertheless, they are better than those reported by Greenhill in his survey of 20 years ago. The results in any series will vary with the type of case done, but it does seem clear that there has been some improvement in the results of this type of surgery and that these operations carry no great risk to the patient. They are worth performing not only from the standpoint of results but from the standpoint of patient satisfaction. There is still much room for technical improvement. At present it would seem that the plastic prosthesis and the opening of the uterus for its insertion presents certain distinct advantages.

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DISTURBANCES OF MICTURITION FOLLOWING WERTHEIM HYSTERECTOMY

BY

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SINCE the end of 1949, all patients presenting at the West Middlesex Hospital with a removable carcinoma of the cervix have been treated by Wertheim hysterectomy. The purpose of this paper is to draw attention to certain disturbances of micturition that sometimes follow Wertheim hysterectomy and can persist for years. These symptoms may be due to removal of much of the nerve supply to the bladder during the course of the operation.

Between March, 1949 and October, 1953, 58 patients had a Wertheim hysterectomy for carcinoma of the cervix. During the same period 23 patients with carcinoma of the body of the uterus were treated by an extended abdominal hysterectomy. In this latter operation the ureters are dissected out; the transverse cervical and utero-sacral ligaments are divided; the bladder is dissected off the upper vagina; and the upper third of the vagina is removed. The post-operative bladder function of these patients has also been assessed.

There is thus a total of 81 patients to consider. The investigation was done at the end of 1953 and the beginning of 1954 and at that time 10 patients were dead and 2 could not be traced. The remaining 69 patients were all seen.

TABLE I
Series Reviewed

	Seen	Dead	Un-traced	Total
Carcinoma of cervix ..	47	9	2	58
Carcinoma of body of uterus	22	1	–	23
Total	69	10	2	81

Retention of urine and some difficulty with micturition is not uncommon after a total hysterectomy and it is almost invariable after Wertheim hysterectomy. It is usual therefore to leave a self-retaining catheter in the bladder after a Wertheim hysterectomy. When this is removed many patients have difficulty with micturition and often fail to empty the bladder completely. Stress incontinence is also common. These immediate post-operative difficulties occur in patients who eventually regain normal bladder function. In this investigation patients have been seen 6 months or longer after operation.

The patient will not complain about changes in bladder function unless they cause her inconvenience so it is necessary to question her directly. The commonest changes in bladder function are loss of the sensation of fullness, difficulty with micturition and stress incontinence.

Loss of the Sensation of Fullness

Of the 69 patients seen 18 had greatly impaired or absent sensation of fullness of the bladder. If this is the only symptom, it may cause the patient no trouble. She often says that she can go all day without emptying her bladder, which presumably becomes stretched. These patients may be aware of the abdominal distension produced by a full bladder.

A number of these patients with loss of sensation find that they leak urine when the bladder is full. They soon learn to avoid accidents by emptying the bladder at frequent intervals although they feel no natural urge to do so. Five patients leaked urine when the bladder was full and at no other time.

Difficulty with Micturition

Twelve patients had difficulty in starting micturition and in emptying the bladder. These patients have to strain, bend forwards or cough in order to start micturition. The stream is poor and intermittent, and emptying the bladder takes a long time.

In a normal person, the abdominal muscles play no part in micturition which is accomplished by the detrusor muscle alone. If this muscle is paralysed or its action is inefficient, as it may be after Wertheim hysterectomy, the patient finds that she must raise the intra-abdominal pressure to empty her bladder. One patient said that passing water was now "like having a baby". Some patients with poor abdominal muscles or a ventral hernia have found it necessary to press on the abdomen during micturition.

Many of these patients empty the bladder incompletely and a residual urine of up to 6 ounces was commonly found. One patient who was operated on in 1950 had complained very bitterly of difficulty ever since the operation, and when seen in 1954 she had 14 ounces of residual urine.

Stress Incontinence

This is a common complaint after Wertheim hysterectomy but as most of the patients are multiparous it is not easy to say whether the operation is entirely responsible. Fourteen patients had stress incontinence that was not present before the hysterectomy. Of these 5 only leak when the bladder is full.

In patients with loss of the sensation of fullness of the bladder, urine entering the urethra is the first indication that the bladder is full. Some of these patients are able to prevent any appreciable leak by contraction of the external sphincter and pelvic floor.

One patient leaks only at night, while the rest are dry at night. In 3 patients the stress incontinence was very severe and seriously limited their activities.

Rectal Symptoms

Although the patients were not questioned as carefully regarding their rectal function, it was noticed that those with marked disturbances of bladder function also have changes in rectal function. They are constipated, rectal sensation is different and deficient and excessive straining is required to empty the rectum.

TABLE II
Disturbances of Micturition

	Carcinoma of Cervix	Carcinoma of Body of Uterus	Total
Loss of sensation ..	16	2	18
Difficulty	11	1	12
Stress incontinence ..	13	1	14
Normal function ..	27	19	46
Total	47	22	69

Note: Most patients with abnormal function had more than one symptom.

LITERATURE

In most papers dealing with the surgical treatment of carcinoma of the cervix there is no reference to any symptoms caused by the operation. If the patient is free from recurrence she is assumed to be well. However, in some recent American papers disturbances of micturition are mentioned and it is evident that they are not uncommon.

In 1944, Meigs noted that patients sometimes had difficulty in emptying the bladder after Wertheim hysterectomy and he thought that this was due to injury to the sympathetic or parasympathetic nerves. In 1950 he again remarked on bladder dysfunctions but at that time he did not think that the symptoms were permanent.

Twombly (1950) also commented that patients have difficulty in completely emptying the bladder after Wertheim hysterectomy. He also considered this to be due to damage to the nerve supply, and expressed surprise that all patients do not have a denervated bladder after this operation.

Brunschwig (1953) thought that atony of the bladder was unavoidable after Wertheim hysterectomy. In some patients it only lasted for a few days, but in a few of his patients it had persisted for 2 years or more. There was also loss of sensation which often remained when

emptying of the bladder had returned to normal.

In April, 1954 Thornton described a series of 33 patients with carcinoma of the cervix who had been treated by Wertheim hysterectomy. Of 28 surviving patients 13 had some micturition difficulties. He mentioned loss of sensation, incontinence of varying degree and large amounts of residual urine as the chief complications, and he attributed them to damage to the parasympathetic nerves. In the discussion that followed this paper, Meigs said that the deep pelvic resection injured the nerve supply to the bladder and he now thought that it was permanent.

Somewhat similar post-operative urinary symptoms have been described after abdomino-perineal resection of the rectum by Williams and Watson (1951). Their patients were men who had complete retention at first, and after a variable period micturition was re-established by straining of the abdominal muscles. There was loss of bladder sensation and a large amount of residual urine. They thought that the symptoms were due to damage to the sacral autonomic fibres as they emerge from the sacral foramina.

Anatomy and Physiology of the Nerve Supply to the Bladder

Anatomy. The bladder receives its nerve supply from the two pelvic or inferior hypogastric plexuses. These contain sympathetic fibres from the last three thoracic and first two lumbar nerves, and parasympathetic fibres from the second, third and fourth sacral nerves. These plexuses are situated on either side of the rectum, cervix and lateral vaginal fornices. Afferent nerves travel with both sympathetic and parasympathetic fibres.

Physiology. Micturition is under the control of the higher centres and stimulation of the parasympathetic nerves causes contraction of the detrusor muscle and emptying of the bladder. Everett (1947) describes the internal sphincter as being part of the detrusor muscle and also under parasympathetic control. During filling of the bladder tonic contraction of the circular fibres at the bladder neck prevents escape of urine. When the detrusor muscle contracts, arches of longitudinal fibres extending into the urethra contract and open the internal urethral orifice. The sympathetic nerves cause vasoconstriction but probably have no effect on micturition.

The Effect of Damage to the Nerves Supplying the Bladder

Presacral Nerve. Division of the presacral nerve containing the sympathetic nerve supply to the bladder may cause transient frequency but micturition rapidly returns to normal.

Sacral Autonomic. Severe damage to the sacral autonomic nerves results in loss of voluntary micturition. After a time the bladder may empty itself automatically but the amount of residual urine is large. There is also loss of the sensation of fullness of the bladder.

Cause of Disturbances of Micturition After Wertheim Hysterectomy

During the course of a Wertheim hysterectomy the pelvic cellular tissue surrounding the cervix and upper vagina is removed, and most of the pelvic plexuses will be removed also. Some fibres travelling with the ureters or vesical arteries may remain intact. The immediate post-operative micturition difficulties are probably due to removal of much of the nerve supply to the bladder. If enough fibres remain intact, normal function returns.

Division of the afferent nerves causes loss of the sensation of fullness, while difficulty with micturition and incomplete emptying of the bladder is probably due to division of parasympathetic fibres.

Most of the patients are multiparous and the stress incontinence might be due to deficiency of the pelvic floor made worse by the operation. However, most of our patients with severe stress incontinence also had loss of sensation or difficulty suggesting that severe nerve damage had occurred.

It was found that micturition symptoms were more common and more severe in patients who had had the complete Wertheim operation for carcinoma of the cervix than in those who had had the modified operation for carcinoma of the body of uterus. Of 22 patients seen after the modified operation 19 had normal bladder function. The remaining 3 each had evidence of nerve damage and the symptoms were mild. In

the modified operation the pelvic glands are not removed and the dissection is not carried as deeply into the pelvis because only the upper third of the vagina is removed. Thus some nerves on the pelvic floor and lateral pelvic walls will escape injury.

It was also found that symptoms were more severe in patients who were left with a short vagina. Sixteen patients had a vagina 1½ inches or less in length and of these 5 had normal and 11 abnormal bladder function. Of 47 patients with a vagina between 2 and 3 inches long, 37 had normal and 10 abnormal bladder function. As a general rule, patients left with a short vagina will have had a more extensive pelvic dissection than those with a vagina 3 inches long. With one exception, patients operated on for carcinoma of the body of uterus were left with a vagina between 2 and 3 inches long.

TABLE III
Relation of Symptoms to Stage of Carcinoma

	Normal Function	Abnormal Function	Total
Stage O	1	1	2
Stage I	12	10	22
Stage II	12	5	17
Stage III	2	4	6
Total	27	20	47
Carcinoma of body of uterus	19	3	22

TABLE IV
Relation of Symptoms to Length of Vagina

	Normal	Abnormal
Vagina 1½ inches or less ..	5	11
Vagina 2–3 inches	37	10

DISCUSSION

Since Wertheim hysterectomy is undertaken for the cure of carcinoma, the extent of the operation must obviously not be limited for fear of damage to the nerve supply of the bladder. After the operation, a careful watch should be kept on the state of distention of the bladder, especially after the catheter is removed. Our patients have improved up to 6 months after operation but after this no appreciable improvement has occurred. Most of the patients become accustomed to their altered bladder function and it is no great inconvenience to them. In this series 3 patients had severe stress incontinence which was responsible for some limitation of their activities. One patient had serious difficulty and complained that she had to spend a lot of time straining to empty her bladder.

We have not been able to improve these patients' symptoms at all. One patient's stress incontinence was so severe that transplantation of her ureters was considered. This was not done, however, as her rectal sensation appeared also to have been impaired by the Wertheim hysterectomy.

SUMMARY

(1) Attention is drawn to disturbances of micturition that commonly follow Wertheim hysterectomy.

These are loss of the sensation of fullness, difficulty and stress incontinence.

(2) It is thought that these symptoms are due to damage to the nerve supply of the bladder.

(3) Improvement occurs during the 6 months after operation but symptoms persisting longer than this are permanent.

ACKNOWLEDGMENTS

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SIRENOMELIA ("MERMAID")

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A RECENT publication (Foulkes and McMurray, 1954) has revived our interest in a case of sireniform malformation observed in 1952. We did not fully appreciate the significance of this malformation for the study of embryology and teratogenesis, nor were we sufficiently aware of its practical obstetrical aspects. Supplementation of the records by photographs giving a clear view of the essential external features of the malformed infant may make the case suitable for publication.

Whilst preparing the report of this case, one of us (H.G.K.) has come across 2 cases of similar malformations. These cases are still being studied, but a summary of the history and relevant findings will be given in this article and will be referred to in the discussion.

The subject of sirenomelia has been repeatedly reviewed. The latest comprehensive survey available to us is that of Kampmeier (1927). Earlier treatises on the subject of sirenomelia were written by Geoffroy St. Hilaire (1836), Förster (1865), Weigert (1878) and Ballantyne (1898). The last named found 120 examples recorded up to his time. Kampmeier collected some 50 additional cases and added one original description. His list of references gives no fewer than 162 publications; of these, one originates in the first century A.D., 6 in the 16th century, 8 in the 17th, 9 in the 18th, 99 in the 19th, and 39 in the early 20th century. This bibliographical achievement commands our admiration.

Of the earlier publications, we draw attention to only one, by Thomas Bartholin (1672), whose father first described the vestibular glands. He lived at a time when even in medical literature facts and fancy were hopelessly intermingled. His own contribution is no exception and he depicts his monstrosity with webbed hands and voluptuous breasts disporting on the waves (Fig. 1). A reviewer exclaims: "If a modern anatomist should evince but an iota of the poetic licence . . . he would stand discredited for the rest of his life" (Kampmeier).

The subject is briefly discussed by Potter (1952) in her textbook. Three cases of her own are shown in illustrations and also one observed by Proshek and Adair. Recent case reports in the British literature were published by Resnick (1945), and by Foulkes and McMurray (1954). The last named authors state that they found only one previous case in the literature but do not cite the reference. Yet in spite of the rarity of this malformation the literature on the subject is by no means scanty.

Case 1

History. Mrs. C.H., a primigravida, aged 35, had been married for 11 years, but pregnancy had been avoided until 3 months before the present conception occurred. She was first seen at the antenatal clinic at the George Eliot Hospital, Nuneaton, on 27th February, 1952, when she stated that her last menstrual period had occurred sometime in October, 1951, but she was unable to remember the exact date. There had been two episodes of slight bleeding some 6 and 7 weeks later; otherwise she had been well during the early weeks of the pregnancy.

On examination, her general condition was satisfactory

and her heart and lungs showed no abnormality. The uterus was enlarged to the size of a 20-weeks pregnancy, and she had recently experienced foetal movements. The foetal heart was not audible. These findings roughly corresponded with the duration of amenorrhoea, and a date in the second half of July was calculated as the expected date of confinement. The blood pressure was 130/80 and the urine free of albumen and sugar. The Wassermann reaction and Kahn test were negative and the blood group was reported to be B, Rhesus negative.

The pregnancy progressed normally apart from a slight tendency to hypertension which was not accompanied by any other signs of toxaemia. The size of the foetus corresponded with the duration of the pregnancy and the foetal position was satisfactory throughout. No X-ray examination was considered necessary during the antenatal period.

On 6th August, the blood pressure was 160/98, and by calculation the pregnancy was estimated to be 2 weeks beyond term. It was therefore decided to admit her for induction of labour and her admission was arranged for the following day. On admission on 7th August, she was found to be in early labour. Labour progressed slowly during the next 24 hours, and, at 5 p.m. on 8th August, the second stage of labour had begun. In spite of good contractions and expulsive efforts, little progress had been made by 6.10 p.m., at which time the foetal heart rate was noted to have fallen to 100/min., indicating some degree of foetal distress. It was therefore decided to complete the delivery with forceps.

Examination under anaesthesia revealed the head to be considerably moulded, in mid cavity in the antero-posterior diameter of the pelvis, with the occiput anterior. The head was delivered without difficulty after an episiotomy had been performed, but some difficulty was experienced with the shoulders. Ergometrine 0·5 mg. was injected intravenously after delivery of the anterior shoulder, but this failed to expel the placenta and manual removal was necessary.

There is no record of when the membranes ruptured, nor of the amount of liquor amnii present. Although slowing of the foetal heart had been noted, there is no record of the passage of meconium.

The infant (Fig. 2) weighed 6 pounds (2·75 kg.) and showed considerable moulding of the head. The lower limbs were fused and there were no obvious external genitalia. The baby survived for about half an hour.

The placenta and membranes were complete and showed no obvious abnormality. They were not sent for pathological examination.

The puerperium was normal and the patient was discharged home on the 10th day.

Mrs. H. attended the antenatal clinic again on 19th October, 1955, giving 8th June, 1955 as the date of her last menstrual period. The pregnancy progressed normally and she was delivered at term of a normal male infant.

X-ray of the malformed infant (Fig. 3). The long bones of the lower extremities are complete and separate; the characteristic medial position of the fibulae is clearly demonstrated. The skeleton of the left foot is fairly complete but the right foot shows fusion of 3 or 4 metatarsal bones; only 3 bony toes can be seen in the film. In the pelvis, there is an apparently normal innominate bone, but the sacrum consists of only 2 segments, which are pointing backwards; the coccygeal bone is absent. No radiological abnormality was found in the upper half skeleton apart from marked moulding of the skull.

Autopsy Findings of the Infant

External. The body is that of a monster of uncertain sex. There is fusion of the lower extremities, but the long bones can be felt to be separate. The common knee-joint is flexed anteriorly and the feet are inverted, the plantar surfaces turned inwards and upwards. The toes are normal in number. No abnormalities of the upper extremities are noticed. A "dimple" is present in the sacral region, and a tuberosity felt underneath it, but there is no evidence of a spina bifida. No anal or urethral opening is present, nor any external genitalia, apart from a small raised "knob" of skin, which might represent a rudimentary penis.

Internal. The internal organs show non-expansion of the lungs, subserous petechiae on the epicardium and engorgement of cerebral vessels. No malformation is found above the diaphragm.

The kidneys are fused at their upper poles, forming a horse-shoe, which is open downwards; two ureters arise from each side. The bladder is small and thick-walled, almost solid. No urethra can be demonstrated.

One testicle is found fairly high up in the abdomen, whilst the other one has entered the inguinal canal.

The colon and rectal stump are distended by meconium, the blind end being hidden in the pelvis.

The bony pelvis is narrow and tapering.

No observations regarding the number and position of the umbilical arteries are recorded, nor is the presence or otherwise of supra-renal glands mentioned in the original post-mortem report.

Histology: A section of kidney shows per-

sistence of considerable amounts of undifferentiated nephrogenic tissue. The glomeruli appear to be diminished in number and the glomerular epithelium is somewhat immature; Bowman's capsules are distended without exception. The tubules, too, present evidence of distension, amounting in some instances to cyst formation.

Case 2

Mrs. K.H., 41 years old and less than one year married, was referred to the antenatal clinic, Birmingham Maternity Hospital, as an elderly primigravida when about 19-weeks pregnant. On examination, a subperitoneal fibroid was found at the fundus, increasing the size of the uterus to that of a 28-weeks pregnancy. Foetal movements had been felt about this time but a few days later they ceased. When the patient was about 23-weeks pregnant, there were repeated small vaginal haemorrhages, so she was admitted to hospital where at 24½ weeks she aborted male twins, apparently of the monochorionic, di-amniotic type.

The placental portion of the first-born twin was rather ischaemic but of fairly normal shape, whilst the other portion was so badly damaged by degeneration and haemorrhage, that the attending midwife described it as a carneous mole.

Both foetuses were badly macerated (Fig. 4); the first-born showed no external signs of malformation (though described as hydrocephalic by the attending midwife): the second one, very much smaller and poorly developed—in fact hardly recognizable as a human foetus—has no upper extremities and a fused and rudimentary lower extremity. In view of very severe maceration no internal dissection was carried out.

X-ray photographs (Fig. 5) of the skeleton were taken and confirmed the absence of upper limbs. The long bones of the lower extremity were surprisingly well developed; again, the fibulae were medial to the tibiae.

The umbilical cord of the malformed twin was sectioned and found to contain only 2 vessels.

Case 3

Mrs. B.C., nearly 28 years old and married for over 4 years had had 2 abortions, each at 9 weeks, in the first and third years of her marriage. She and her husband had undergone investigation at the Sub-fertility Clinic, Women's Hospital, Birmingham. When pregnancy was established, Mrs. C. was referred to the antenatal clinic, Birmingham Maternity Hospital.

Throughout the pregnancy, the fundus was higher than expected from the dates. Mrs. C. went into labour at 29 weeks by dates (fundal height: 34 weeks) and was admitted as an emergency, with a fully dilated cervix. The membranes had ruptured prior to admission but the patient could not tell when this had happened.

A limb presented, with a loop of pulsating cord anterior to it. Delivery by breech extraction of a stillborn infant followed (Fig. 6). The placenta was manually removed and was reported as normal: it was not examined by the pathologist.

X-ray findings (Fig. 7). There is severe scoliosis of the lumbar spine with a deformed and rudimentary pelvis and absence of the left lower limb. Only one bone is present below the knee. The right femur is normal in its upper half but the distal portion is abnormally widened; the lower epiphysis shows two centres of ossification.

Autopsy Findings of Infant

External. The body is that of a monster of uncertain sex. There is no abnormality of the upper extremity but only one lower limb is present, which is right of the mid line and consists of a fairly well-shaped thigh to which is attached a rudimentary leg, rather short and tapering and containing only one bone. No foot is present. There is no evidence of external genitalia, urethra or anus.

Internal. There is no malformation above the diaphragm. The colon ends blindly and there is evidence of incomplete intestinal rotation. The kidneys are absent and the suprarenal glands are unfolded and flat, occupying as large an area as is usually covered by the kidneys. No ureters are present nor any structure resembling the urinary bladder. There is only one umbilical artery which communicates directly with the abdominal aorta. Ovaries, Fallopian tubes and rudimentary uterine horns are present. The bony pelvis is grossly deformed.

Comment

There is no evidence of fusion of the lower extremities as in the true sirens, the malformation being clearly asymmetrical. There is, however, nothing to suggest intra-uterine "amputation" of the left lower limb and therefore the malformation is regarded as "sirenoid". This view is strengthened by the presence of a single umbilical artery and associated malformations, viz., absence of urinary tract, defect

of intestinal tract, absence of orifices and bony defects. It might be labelled as a combined hemimelia (distal stunting) and ectromelia (total absence of an extremity).

Subsequent history. Mrs. C. is again pregnant, the delivery being expected on 6th October, 1956. At 35 weeks no skeletal deformity is seen on X-ray examination.

Discussion

Sex. In the first case under discussion, this was established by a demonstration of undescended testicles. Contrary to popular belief the majority of mermaids have male gonads: In Kampmeier's series, out of a total of 52 cases in which the sex was determined, 38 were males. In most reported cases there were no obvious external genitalia and this probably led to the belief that these creatures were feminine. Newbill (1941) described a sireniform infant who differed from the great majority in having a well-developed penis and a scrotum but the testes were undescended. A rudimentary penis, in front of the fused thighs, was found in our first case as well as in a number of others. In one recorded case, a penis arose from the posterior aspect. We have not sectioned the rudimentary penis but other authors have done so and found corpora cavernosa or other histological confirmation.

The foetus in Case 2 is believed to have been male because its apparently uniovular twin brother had male external genitalia.

In Case 3, ovaries, Fallopian tubes and rudimentary uterine horns were clearly demonstrated.

No genital, urethral or anal orifice was present in any of the described cases nor in the infants reported by Resnick (1945) and by Foulkes and McMurray (1954). Newbill's (1941) case had a urethral canal in the penis, communicating with the uro-genital sinus.

Malformations of the upper urinary tract are recorded in the great majority of the reported cases and a considerable variety of conditions has been described. The most common finding is complete absence of both kidneys and ureters which adds the features of renal aplasia to those of sirenomelia. This combination has been discussed by Fritzche (1955) in a recent paper, and was also observed in Case 3. In the first case, there was fusion of the upper poles of the kidney (horse-shoe kidney),* associated with doubling of the ureters. Such a condition has to our knowledge not been reported in any other case of sirenomelia. The histological picture of the kidneys in this case shows that they were rather immature and probably non-functioning.

Amniotic fluid. No record was found in the notes of Case 1 regarding rupture of the membranes and amount of amniotic fluid. Positive and explicit statements of oligo-hydramnios are relatively rarely obtained in clinical records and it is probably fair to assume that where neither the patient nor her attendants notice the escape of fluid, no record would be made. This was so in Case 3; there, too, no direct information was obtained from the case notes but subsequent questioning established absence of amniotic fluid. Oligo-hydramnios is the rule in those cases that are associated with renal aplasia and might be expected when there is no urethral orifice, irrespective of the severity of the malformation of the upper urinary tract.

Lack of amniotic fluid is regarded as the mechanical cause of minor malformations of the extremities, such as talipes. It has been suggested that oligo-hydramnios also plays an aetiological part in the causation of sirenomelia but we find it very hard to accept this suggestion.

Incomplete rotation of the legs is a constant finding in all cases of symmelia where the lower extremities show no gross bony deficiency. In these cases an X-ray diagnosis of the malformation *in utero* is possible because the fibulae are medial to the tibiae (Resnick, 1945). The peculiar fish-tail shape of the feet is due to this incomplete rotation.

Single umbilical artery. No record of number and topography of the umbilical arteries was made in the first case under discussion, but in both cases observed at the Birmingham Maternity Hospital a single umbilical artery was present. Kampmeier (1927) stresses this single artery as the essential feature of sirenomelia and attributes to it some aetiological significance.

* This type of horse-shoe kidney is very rare: see G. Gordon-Taylor (1936): "On horse shoes and horse-shoe kidney concave downwards", *Brit. J. Urol.*, **8**, 112.

FIG. 1
Reproduction of illustration in case report of Thomas Bartholin.

FIG. 2
Case 1. Fusion of lower limbs, incomplete rotation of feet and rudimentary penis.

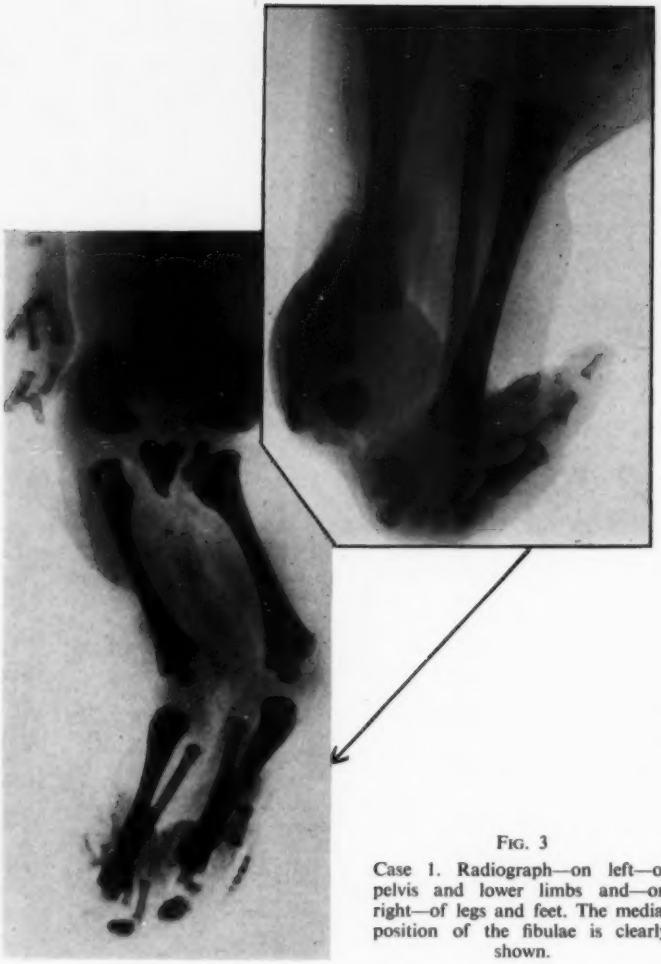

FIG. 3

Case 1. Radiograph—on left—of pelvis and lower limbs and—on right—of legs and feet. The medial position of the fibulae is clearly shown.

FIG. 4

Case 2. Uni-ovular twin pregnancy. The malformed sireniform foetus looks almost amorphous. (The X-ray in Fig. 5, however, shows a well formed skeleton.)

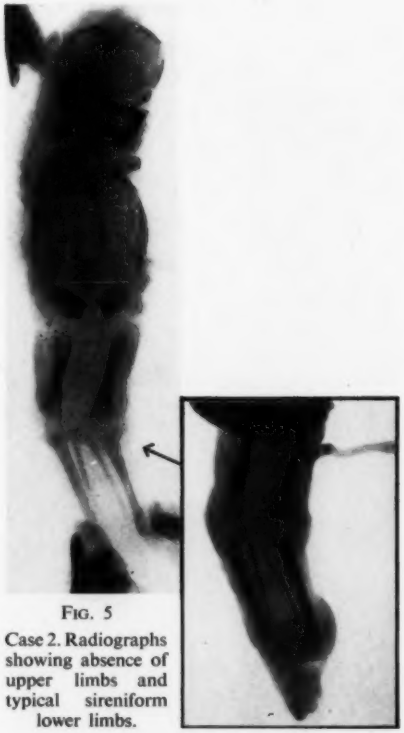

FIG. 5

Case 2. Radiographs showing absence of upper limbs and typical sireniform lower limbs.

FIG. 7
Case 3. Radiographs showing stunted bones of a single lower limb.

FIG. 6
Case 3. Sirenoid foetus: asymmetrical.

D.W.H., H.G.K.

Weigert (1886) and later authors regard this vessel, which connects directly with the abdominal aorta, as a persistent vitelline or omphalo-mesenteric artery.

A single umbilical artery may occur in otherwise normal infants or in association with malformations other than symmelia. It is significant that in a series of 14 cases of single umbilical artery examined by Hyrtl (1870), all were males.

Parental sub-fertility, maternal age and parity. Malformations are popularly attributed to parental sub-fertility, but the statistical facts available are inconclusive. The first case is associated with a long history of voluntary infertility and occurred in an elderly primipara. The 2 cases at the Birmingham Maternity Hospital both occurred in primiparae. The first of these happened in a woman of 41, who had, however, only been married for about 1 year, and in the second Birmingham case the parents had attended the sub-fertility clinic and the father was known to have some degree of oligospermia. Foulkes and McMurray (1954) suggest that sub-fertility might have been a factor in their case, but do not produce any definite evidence. Their patient also was an elderly primipara.

Resnick's case (1945) occurred in a primigravida aged 24. In Newbill's case (1941), the mother was apparently primiparous though her age is not stated. Fritzche's (1955) patient was a primigravida of 19. As far as is known to us, the mothers in all the cases reported since Kampmeier's review were primiparous, but their ages range from 19 to 41.

Kampmeier, who has tabulated the findings in 79 cases, reports that 20 of these monsters were born to multiparous mothers. A greater incidence of malformations in primiparous women is well known, but it seems that they do not have any monopoly of giving birth to sireniform monsters.

Experimental teratogenesis. We cannot discuss here the problem of aetiology nor the validity of deductions from experimental malformations. Experimental production of monsters has been a method of embryological research for several generations.

We wish, however, to draw attention to the production of symmelia in chick embryos by irradiation of the posterior end of the body at the stage of the primitive streak (Wolff, 1936). This resulted not only in fusion of the legs, but also in defects of the uro-genital system, comparable with those of the spontaneous malformations in humans.

Summary

A case of sireniform malformation is described. The summary findings in 2 similar cases are recorded. The essential features are briefly discussed and some of the literature is referred to.

Acknowledgments

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SARCOIDOSIS OF THE FALLOPIAN TUBES

Report of a Case

BY

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DESPITE the extensive literature on sarcoidosis there are surprisingly few references to involvement of the female reproductive organs and we have found none to a case of sarcoidosis of the Fallopian tubes diagnosed during life. The present case is reported because of its apparent rarity.

CASE REPORT

The patient, when first seen by a gynaecologist in February, 1949, was 24 years old. She had been married for 18 months and was admitted to hospital for investigation and treatment of dyspareunia. Pelvic examination under anaesthesia revealed no abnormality and she was treated by manual stretching of the vagina.

In June, 1949, she was again investigated in hospital because of recurrent attacks of frequency of micturition and dysuria. A catheter specimen of urine, intravenous pyelography, cystoscopy and further gynaecological examination showed no abnormality.

In May, 1953, she was seen because of sterility for the past 4 years. She also complained of tiredness and irritability, right sided abdominal pain and a yellow vaginal discharge. Menstruation was regular, occurring at 18- to 28-day intervals, and lasting usually for 10 days, associated with moderately severe dysmenorrhoea. Vaginal examination showed the uterus to be anteverted, small and mobile, and there was now felt for the first time a large mass in the posterior fornix. It was not tender and was thought to be an ovarian cyst.

She was admitted to hospital and on 29th May, 1953, prior to laparotomy, had a bimanual examination under anaesthesia. The perineum, vulva and vagina were normal; there was a pin-hole os, and the cervix was difficult to mobilize; the uterus was acutely anteverted and it was difficult to determine its outline and relation to the adnexa. A large indefinite mass was again palpated in the posterior and right fornices and it was not possible to define the tubes and ovaries. Dilatation and curettage were attempted but the cervix was rigid and some difficulty was experienced; a false passage was made with perforation of the uterus and no curettings were obtained.

Laparotomy was immediately performed through a lower mid-line incision. Miliary nodules were seen involving the bowel wall and parietal peritoneum. Both Fallopian tubes were grossly distended and retort shaped, and their serous coat studded with nodules. The ovaries were adherent to the tubes and back of the broad ligaments. There was a large ovarian abscess some 9 centimetres in diameter on the right and many dense adhesions involved tubes, uterus and ovaries in an inextricable mass. Diagrammatic representation of the appearance seen at operation was made by the surgeon at the time (Fig. 1).

A biopsy was taken of the omentum on which there were nodules. Any further operative interference was deemed inadvisable. The histological report was: "Small nodule of omental adipose tissue with a localized foreign body giant cell reaction on its surface. There is no evidence of tuberculosis and no optically active material can be demonstrated under the polarizing microscope" (Fig. 2 (*a*) and (*b*)).

The gross appearance at operation was considered to be characteristic of tuberculosis and treatment was instituted with daily intramuscular injections of 1 g. of Streptomycin in

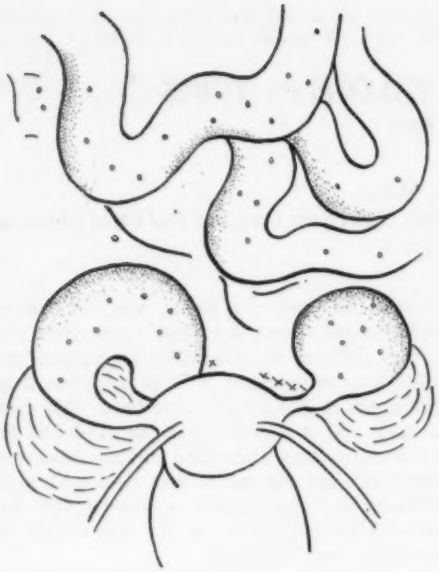


FIG. 1

Diagrammatic representation of the appearance at operation from a sketch made by the surgeon at the time. It shows the bilateral pyosalpinx, ovarian abscesses and miliary nodules on the bowel and omentum.

association with 20 g. of P.A.S. in divided doses by mouth. This was continued until a total of 48 g. of Streptomycin had been reached by July, 1953, when the patient was transferred to a convalescent home. Vaginal examination at that time gave the impression that the condition in her pelvis was resolving.

Because of the diagnosis of pelvic tuberculosis, the patient, on her return from convalescence, was referred to the Windsor Chest Clinic for routine examination. X-ray of her chest taken on the 18th June, 1953, i.e., shortly after the laparotomy, was thought to be within the normal range, but re-scrutiny, because of subsequent developments showed that there was bilateral hilar enlargement with fine reticular shadows radiating from the right hilum into the lower lung field (Fig. 3). These shadows became more pronounced and, in September, 1954, the left lung parenchyma was also involved.

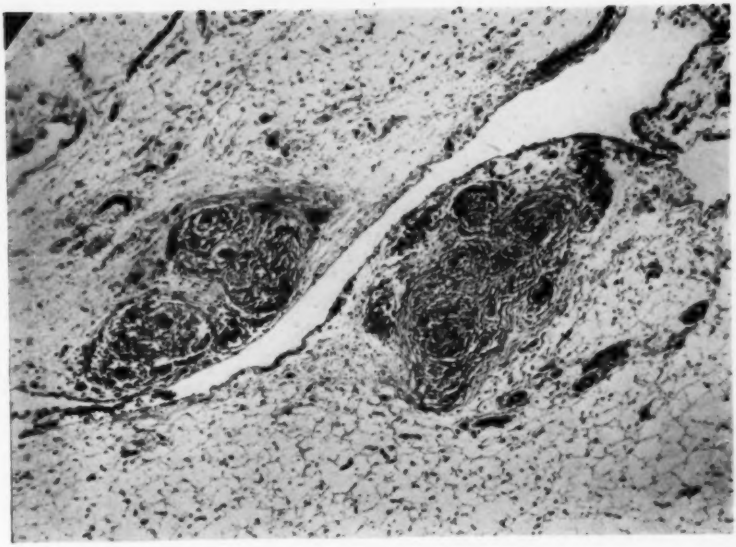
By January, 1955, X-ray showed extensive nodulation in the lower zones of both lungs with evidence of right middle lobe collapse. There was a marked lack of constitutional disturbance and complete absence of cough and sputum, despite the extensive radiological changes. In view of her pelvic condition it was thought that the picture was part of a disseminated tuberculosis, and chemotherapy was re-instituted. The patient was allowed to pursue her normal activities as a housewife and part-time shop assistant and for 2 months given Streptomycin 1 g. twice weekly with Isoniazid 400 mg. daily, followed by a period of 4 months during which P.A.S. 18 g. daily replaced the Streptomycin.

The chemotherapy was discontinued in July, 1955, as it was producing no obvious effect on the abnormal X-ray appearance of the lungs. These, if anything, were becoming more extensive, particularly in the left lung field (Fig. 4). By now it was becoming increasingly manifest that the distribution of the disease shadows, their lack of response to adequate chemotherapy, and the absence of constitutional disturbance made a diagnosis of pulmonary tuberculosis unlikely. Sputum examination and laryngeal swabs were repeatedly negative for *Mycobacterium tuberculosis*, both by direct microscopy and culture. Tuberculin tests using undilute Old Tuberculin with the Heaf Multiple Puncture apparatus and 1 in 100 Old Tuberculin (100 I.T.U.) in the Mantoux test were repeatedly negative; plasma proteins were: total protein 5·0 g. per cent; albumen 3·8 g. per cent; globulin 1·2 g. per cent.

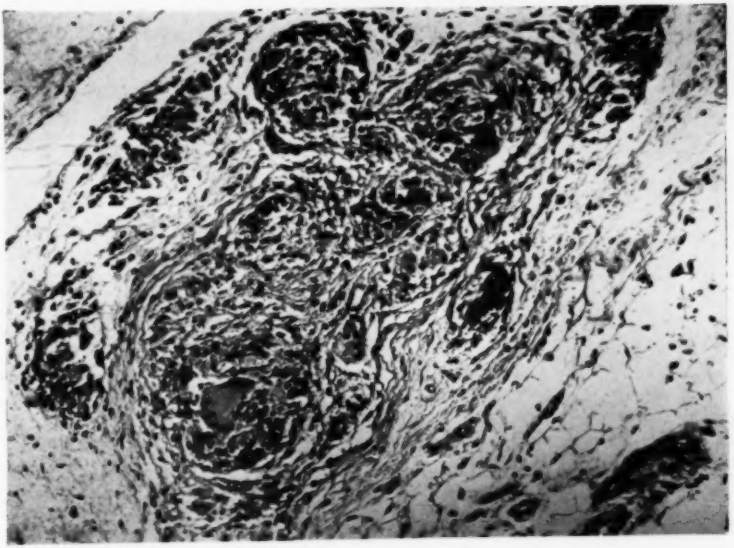
When last examined in September, 1955, the patient was very well. She had no symptoms or signs referable to her respiratory tract despite the persistent nodular shadows in the mid and lower zones of both lung fields. Her only complaint was of slight dyspareunia. Her menstrual cycle was normal and examination revealed the persistence of a cystic mass in the left pelvis with a fullness on the right side. There was some enlargement of the spleen.

DISCUSSION

The only unequivocal case of sarcoidosis of the Fallopian tubes I have been able to find in the literature is in an article by Cowdell (1954). The tubal involvement was found at autopsy in



(*a*) ×60



(*b*) ×150

FIG. 2 (*a*) and (*b*)

Omental Biopsy. Epithelioid tubercles clearly defined within the fatty omental tissue, with only slight round cell infiltration in their vicinity, without central caseation, and showing several Langhans-type giant cells.

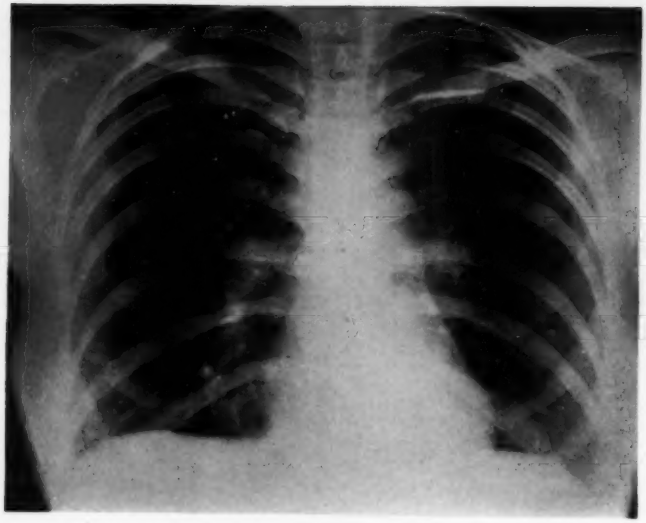


FIG. 3

X-ray of chest taken in June, 1953, shortly after the laparotomy. It shows bilateral hilar enlargement with fine reticulation radiating into the mid zone from the right hilar region.

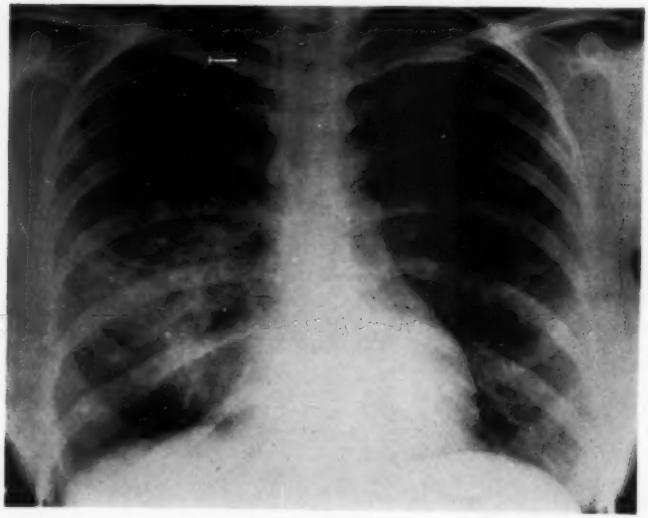


FIG. 4

X-ray of chest taken in August, 1955. It shows more extensive changes, with scattered mottling in the left mid zone and dense confluent shadows in the right mid and lower zones.

S.K.

a young woman who died suddenly of heart block due to cardiac sarcoidosis. There was no information on her previous menstrual history.

Reference to involvement of any part of the female reproductive organs is remarkably infrequent. In his monograph on sarcoidosis Leitner (1949) gives only two references to uterine sarcoidosis. One is to an article by Engelhard (1946), who describes 2 cases diagnosed on curettage, both having associated changes elsewhere in the body. The other is to the paper of Garland and Thompson (1933), who describe the autopsy of a 28-years-old patient who had miliary involvement of the peritoneum and miliary tubercles on the serous surface of the uterus. The ovaries and tubes appeared normal to the naked eye. Longcope (1941) lists, in a table, a case of endometrial involvement, but does not enlarge on it. A sentence, probably about the same case, appears on page 70 of the exhaustive review of Longcope and Freiman (1952). The patient had known sarcoidosis and menorrhagia, and curettage revealed many epithelioid granulomata.

It is surprising that so few cases have been described in view of the well-known tendency for the lesions of sarcoidosis to be widely disseminated throughout the body. Almost every part of the body has been found to be involved and has been described in the voluminous literature on the disease (Pinner, 1938; Rubin and Pinner, 1944; Pautrier, 1948; Leitner, 1949; Longcope and Freiman, 1952). It is difficult to be sure of the incidence of sarcoidosis, but cases of lung involvement are certainly not uncommon in the experience of most chest physicians. The condition, of which a clear cut definition is by no means easy, is becoming increasingly well recognized as more is learnt about its clinical manifestations and histological appearance (Scadding, 1950).

While there is still much controversy as to the aetiological basis of the disease most authorities agree on the resemblance of many of the lesions to those caused by tuberculosis. Some of the early references to the condition described it as non-caseating tuberculosis (Pinner, 1938), and indeed the aspect of the pelvic organs at laparotomy in the present case showed changes strikingly similar to those seen in cases with widespread tuberculous involvement. However, the omental biopsy of a miliary nodule taken at the time of laparotomy showed a histological picture rather more consistent with a diagnosis of sarcoidosis. It was noteworthy that there was no evidence of caseation, a feature which would have been expected if the extensive and advanced changes in the pelvic organs represented caseating tuberculosis.

The changes in the lungs as demonstrated on X-ray add further support to the diagnosis of sarcoidosis. These corresponded well to the appearance described by Scadding (1950) as being characteristic of the condition. There was a bilateral hilar lymph node enlargement accompanied by a fine diffuse pulmonary infiltration in the right lung which was present at the time of laparotomy. This was followed by a coarser irregular mottling which ultimately spread to involve the left lung. Coincident with these changes there was remarkably little constitutional disturbance, the E.S.R. was within the range of normality, sputum tests were repeatedly negative as were tuberculin skin tests using up to 100 International Tuberculin Units.

It seems evident that diagnosis on gynaecological examination alone would not have been possible. The clinical picture was indistinguishable from that of pelvic tuberculosis in its insidious onset, vague symptoms of pain, leucorrhoea and sterility and physical signs of indefinite swelling in the fornices. It is the opinion of Cowdell (personal communication) that primary diagnosis even from a resected tube is not easy, as it is a situation where a variety of granulomata may arise (Roberts, 1947). Tubal tuberculosis may simulate sarcoidosis as in some of the photographs in an article by Potts (1951), and Cowdell has seen sundry foreign body granulomata of this site, some probably due to oily injections or talc, and others of unknown origin which can be most confusing in their similarity.

Summary

Description is given of a case of sarcoidosis of the Fallopian tubes with associated changes in the ovaries, peritoneum and lungs.

Reference is made to the literature to illustrate the scarcity of recorded cases.

Note is made of the failure of antituberculous chemotherapy to affect the course of the condition and of some features in its diagnosis.

Thanks are due to Dr. L. E. Glynn of the Canadian Red Cross Memorial Hospital, Taplow, for considerable help in the preparation of this paper, to Mr. H. Love, former obstetric registrar at the same hospital for his diagram of the appearances at laparotomy, and to Mr. D. Maxwell and Dr. Brian Thompson, under whose care the patient was treated. The photographs were prepared by Mr. P. Fisk of the photographic department of the Canadian Red Cross Memorial Hospital.

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THE EFFECT OF MATERNAL ANOXAEMIA ON THE FOETAL HAEMOGLOBIN OF THE NEWBORN

BY

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FOETAL haemoglobin is a distinct form of haemoglobin differing from that of the adult by its different oxygen and carbon dioxide affinity (Darling, Smith, Asmussen and Cohen, 1941; Eastman, Ceiling and DeLawder, 1933), its greater resistance to alkali, different solubility, chemical structure (Porter and Sanger, 1948), immunological properties (Chernoff, 1952; Darrow, Novakovsky and Austin, 1940) and electrophoretic mobility (Andersch, Wilson and Menten, 1944; Beaven, Hock and Holiday, 1951).

The outstanding feature of foetal haemoglobin is its greater affinity for oxygen which is supplied at low tension in the placenta. The synthesis of foetal haemoglobin seems to occur both in bone marrow and extramedullary centres of haematopoiesis (Schulman and Smith, 1954). The adult type of haemoglobin begins to replace the foetal during the last trimester of pregnancy, the concentration of foetal haemoglobin being about 90 per cent at the 36th week and about 80 per cent at term (Walker and Turnbull, 1955). Foetal haemoglobin decreases gradually after birth and reaches 70 per cent at 2 weeks, 50 per cent at 4 weeks and may persist in significant amount up to the 30th month of age (Schulman and Smith, 1954).

This foetal type of haemoglobin may sometimes appear in persistent anoxic conditions in adults such as in persons living at high altitudes (Hoffman, 1954), in patients with sickle cell anaemia (Singer, Chernoff and Singer, 1951) and in rare cases of severe persistent bronchial asthma and cor pulmonale (Abrahamov, to be published).

Such observations suggest that anoxic conditions of the foetus might induce increased production of foetal haemoglobin or delay the appearance of the adult form. Anoxia in the foetus may arise in conditions which interfere (1) with oxygenation of the foetal blood in the placenta, (2) with the passage of blood from placenta to foetus and (3) in maternal diseases in which the oxygen content of the blood is chronically lowered.

The following observations demonstrate that, of these possibilities in the foetus at term, abnormally high foetal haemoglobin levels are found only in newborns delivered of mothers in whom the oxygen blood content is decreased.

MATERIAL AND METHODS

Control series. Foetal haemoglobin concentrations were determined in umbilical vein blood, collected from 100 full-time newborns. The mothers consisted of healthy pregnant women, who had an uneventful labour at term with delivery of normal infants without asphyxia. The birth weights ranged from 2,500–4,000 g. (Fig. 1).

Anoxaemia arising during labour. Foetal haemoglobin concentrations were determined in 3 newborns delivered abdominally because of premature separation of the placenta, and in 9 cases of neonatal asphyxia (3 cases of prolapse of cord, 2 cases of prolonged labour and 4 cases of entanglements and true knots of the cord—Fig. 1).

Chronic maternal anoxia. This group consists of 12 newborns, delivered from mothers suffering from chronic diseases with low blood oxygen

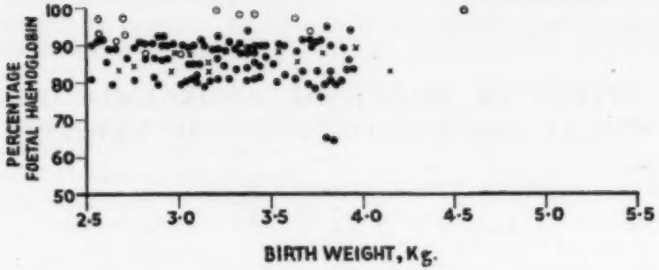

FIG. 1

Foetal haemoglobin concentration in full-time newborns in relationship to birth-weights.

(•) Normal. (×) Suffering from asphyxia. (°) Delivered by anoxaemic mothers.

content, such as heart failure (4 cases), severe bronchial asthma with cyanosis (2 cases) and severe anaemia (6 cases, Fig. 1).

Foetal haemoglobin determinations were made according to the method described by Singer, Chernoff and Singer (1951).

RESULTS

(1) The foetal haemoglobin content of the blood of 100 normal full-time infants varied from 64·1 per cent to 95 per cent, with an average of 86·5 per cent (standard deviation 5·62, standard error 0·56, coefficient of variation 0·07).

(2) Newborns suffering from anoxia during labour, such as in premature separation of placenta, in prolonged labour and in cord entanglements, showed foetal haemoglobin values within the normal range (see Fig. 1).

(3) In 10 out of 12 cases of chronic anoxaemic conditions in pregnancy, foetal haemoglobin of the newborns was above the normal and varied from 94·5 per cent up to 100 per cent. Four of the mothers suffered from congestive heart failure and their percentage foetal haemoglobin values were 94·5, 94·5, 98 and 100. Two were affected by bronchial asthma with cyanosis and the values were 98 and 100. Infants delivered of mothers with severe chronic anaemia had abnormally high foetal haemoglobin values in 6 cases and normal levels in 2 cases. Although no reason could be found for these normal values, in both mothers the red cell count was not excessively low (3·6 and 3·0 million), but the MCV was greatly reduced (78·7 and 66·4) (see Fig. 1).

DISCUSSION

The results obtained in this study indicate that the oxygen content of the maternal blood may influence the foetal haemoglobin concentration in the newborn. The decrease of the blood oxygen level in the maternal circulation induced by chronic anoxic conditions, such as heart disease with persistent dyspnoea, with cyanosis or severe long standing anaemia, seems to delay the production of adult type of haemoglobin in the foetus. It has been shown that the adult type of haemoglobin replaces the foetal form from the 8th month of pregnancy and reaches a concentration of about 20 per cent of total haemoglobin at birth. Following delivery and the establishment of pulmonary respiration with sudden increase of oxygen supply to the newborn, the foetal type of haemoglobin is gradually replaced by the adult form.

In anoxic conditions arising during pregnancy and labour, the foetus overcomes the reduced oxygen supply by increased bone marrow activity and haemoglobin production. The high foetal haemoglobin concentration in newborn children of anoxic mothers constitutes another mechanism of foetal adaptation to the low oxygen blood content. In severe maternal anoxia persisting throughout the whole course of pregnancy, the foetal haemoglobin concentration approaches, and may even reach, 100 per cent.

It should be noted that follow-up of the foetal haemoglobin in these infants showed a normal course of replacement by the adult type of haemoglobin. The high content of foetal haemoglobin in the infants born of anoxaemic mothers may explain why none of them suffered from asphyxia at birth. It is of interest that the foetal haemoglobin concentration is not increased in infants suffering from anoxia at birth due to complications arising during labour (Fig. 1). It might be possible therefore that the production of adult haemoglobin by the foetus is delayed only in those conditions in which oxygen supply to the foetus is chronically reduced for a considerable part of pregnancy.

Summary

In order to determine whether reduced oxygen supply to the foetus influences the foetal haemoglobin concentration, foetal haemoglobin values on cord blood of normal full-time infants were compared with those found in conditions leading to foetal anoxia. The percentage values obtained in 100 normal infants varied from 64·1 to 95, with an average of 86·5. In 12 newborns suffering from asphyxia due to complications arising during labour, normal foetal haemoglobin values were found. In 10 out of 12 newborns delivered of mothers with chronically lowered oxygen blood content abnormally high foetal haemoglobin concentrations were observed, varying from 94·5 up to 100 per cent. It is assumed that the high foetal haemoglobin concentration in newborns of anoxaemic mothers is due to the adaptation of the foetus to the chronically reduced oxygen supply.

We are indebted to Dr. G. Kallner and Mr. Dror from the Central Bureau of Statistics of the Government of Israel, for the statistical analysis quoted in this paper.

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THE CLINICAL USE OF RADIOLOGY IN PLACENTA PRAEVIA

A Review of 433 Cases of Ante-partum Haemorrhage Examined Radiologically (1951–1954)

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DURING recent years radiology has assumed increasing importance in the diagnosis and management of placenta praevia by localizing the placental site. In the Simpson Memorial Maternity Pavilion a 4-year follow-up and review of all cases X-rayed for possible placenta praevia has been completed and an attempt to correlate the radiological report with the subsequent obstetrical findings has been made. Several interesting features have been revealed by this review and these are presented in this report.

A marked increase in the utilization of radiology in the diagnosis of placenta praevia is immediately apparent. In 1951, of the 140 cases of ante-partum haemorrhage admitted to hospital, 71 cases were X-rayed whereas in 1954, out of the 149 admissions for ante-partum haemorrhage, 138 cases were investigated radiologically. The total admissions to the hospital for these years were 4,132 and 4,253 cases respectively.

There were a number of cases of proved placenta praevia which were not X-rayed, although in-patients for varying periods prior to delivery, and these are shown in Figure 1. In 1950 there were 14 such patients in hospital for an average of 11 days before delivery. The number of cases in this category gradually dropped, until in 1953 there were only 2 patients who were not X-rayed and these were in hospital for only 1 or 2 hours before delivery. In 1954 the figures were 4 cases with an average of 3 hours hospitalization. In the latter cases the severity of bleeding created an emergency and suggested the probable clinical diagnosis of placenta praevia. It was considered that any delay in dealing with the emergency in order to permit an X-ray examination was unjustifiable.

Another interesting feature revealed in this study concerned the estimated period of gestation at which time the radiological diagnosis of placenta praevia was made, and subsequently confirmed on clinical evidence. This is shown in Figure 2.

In 1952 most cases of ante-partum haemorrhage were X-rayed at or near term, whereas in 1954 the majority were X-rayed at or about 32 weeks. This difference indicated the increasing use of radiological examination as a means of planning the management of cases of ante-partum haemorrhage by the obstetrician. Patients admitted to hospital with ante-partum haemorrhage are examined radiologically at the earliest opportunity and in many cases their stay in hospital can be reduced when placenta praevia is excluded. Placenta praevia is difficult to diagnose or exclude radiologically before the foetus has attained an estimated maturity of 32 weeks. The findings of radiological examinations carried out before this time are usually verified by re-examination after the 32nd week.

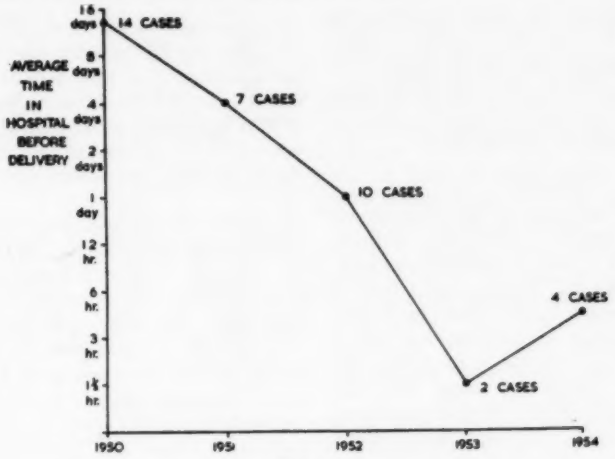

FIG. 1

Number of cases of placenta praevia not X-rayed and with average time in hospital before delivery.

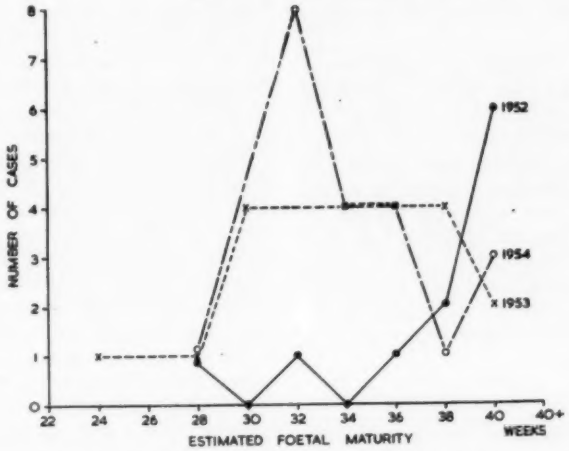

FIG. 2

Estimated period of gestation at which placenta praevia was diagnosed radiologically.

It is not intended that this paper should include full details of radiological technique. The principle underlying modern technique however must be appreciated by the clinician if he is to understand the X-ray report. The principle is simple; the placenta occupies space. Where there is no space available there is therefore no placenta; where there is space available it is possibly occupied by the placenta. In investigating a patient in whom placenta praevia is suspected an attempt is firstly made to show that there is no space between the presenting

part and the brim of the pelvis and thereby placenta praevia is excluded. If there is space between the presenting part and the brim of the pelvis, other explanations, such as full bladder, full rectum, soft tissue tumours, etc., must be considered and excluded if possible.

Technique

The technique adopted in the Department relies entirely on straight radiography with the foetus acting as if it were a contrast medium. The uterus, placenta and liquor amnii are all of the same radiographic density, but the foetus, which is of a higher specific gravity, has a different radiographic density in its bones and subcutaneous fat. Views are taken with the patient in such a position that the foetus is above the suspected soft tissue shadow. Under gravity the foetus will sink to the most dependent part displacing any liquor amnii but not displacing the placenta. This soft tissue technique has been described in various publications (Whitehead, 1953; Reid, 1949, 1952, 1953) to which readers may refer for details.

Difficulties arise when there is a relative excess of liquor amnii masking the placenta as in early pregnancy and in hydramnios. Extrinsic soft tissue masses are confusing and it is therefore important that the bladder and rectum be emptied prior to radiological examination. Other soft tissue masses, such as uterine fibroids or ovarian cysts, simulate the placenta and their presence can only be suspected radiologically by their shape and position. When these complications are not present the information obtained from the radiological examination is definite and reliable.

Radiological Classification

The classification which we have now adopted in reporting placenta praevia is shown in Figure 3. The lower uterine segment in the latter months of pregnancy is considered to lie at the pelvic brim posteriorly and about 1 inch above the brim anteriorly. In Type I placenta praevia the mass of the placenta is above the brim with the margin dipping down into the pelvis slightly displacing the presenting part. Anteriorly there may be normal separation of the foetus from the symphysis, but when the main mass of the

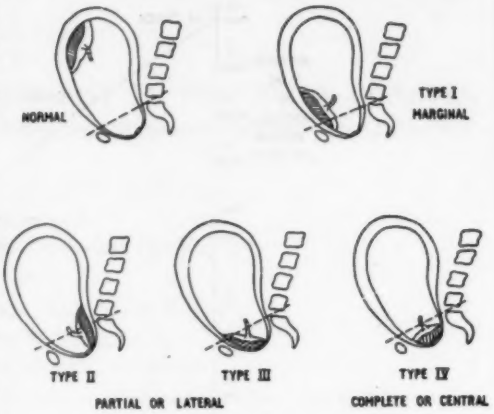

Fig. 3
Classification of placenta praevia.

placenta is immediately above the brim it is considered to be a Type I placenta praevia. In Type II placenta praevia the mass of the placenta is at the brim with the margin unlikely to extend as far as the internal os. In Type III the mass of the placenta is slightly below the brim with the margin probably covering the internal os. In Type IV the mass of the placenta is in the pelvis.

Radiological typing is thus determined by the position of the mass of the placenta in contrast to obstetrical classifications which are determined by the position of the margin of the placenta. This difference is due to the fact that it is not possible to visualize the placental margins radiologically except when calcification is evident. Radiological and clinical classifications therefore may not always agree but the discrepancy should not be greater than one type. The greatest difficulties in discrimination are between Type I and no placenta praevia, and between Type II and Type III placenta praevia.

Review and Follow-up

All cases X-rayed for possible placenta praevia during the 4-year period 1951 to 1954 were reviewed. The X-ray report made at the time of the radiological examination was correlated with the final clinical diagnosis which is made by a senior member of the obstetrical staff.

The results fall into three main groups: placenta praevia not present; definite placenta praevia Types II, III and IV; indefinite or uncertain placenta praevia. These latter cases were variously reported; Type I, possibly Type I, or possibly Type I or II. Altogether 433 cases were X-rayed in this period and these are listed in Figure 4.

The first group to be considered consists of 296 cases where the radiological examination reported "no placenta praevia". Scrutiny of case records revealed that in 293 cases placenta praevia was excluded clinically. The remaining 3 were classified obstetrically as placenta praevia. The first case, a Type II posterior, showed at the radiological examination an abnormal quantity of gas in the rectum and this was accepted as the cause for separation of the foetus from the promontory. The other 2 were Type I, 1 of which revealed a definite soft tissue shadow immediately above the pubic symphysis in the lateral film. This would now be reported as a Type I anterior placenta praevia. Thus radiology can show almost 100 per cent accuracy in excluding placenta praevia.

In the group reported radiologically as possibly Type I, Type I, or possibly Type I or II placenta praevia the difficulty in differentiating Type I and no placenta praevia is shown. In many cases of radiologically Type I placenta praevia there is no clinical indication for exploration of the lower uterine segment as the patient commences labour spontaneously without recurrence of bleeding. Thus in many instances there is no means of verifying the radiological opinion.

The group reported Type II, III or IV is shown in more detail in Figure 5. From this Figure it will be seen that in all a total of 54 cases were reported Type II, III, or IV placenta praevia and of these 42 cases were "confirmed". The term confirmed means that the case had been reported radiologically as the same type of placenta praevia as was subsequently classified obstetrically or was accurate to within one type. The 12 cases which were not placenta praevia demonstrate the difficulties which we have previously mentioned. In some cases the radiological examination was incomplete. This was often due to the patient being unable to stand during the examination. Malpresentation was sometimes found and in such cases it was not possible to exclude the presence of placenta praevia. In these cases it was suggested that further films be taken when the condition of the patient improved or after correction of the malpresentation. If these further films had been taken they would probably have confirmed or excluded placenta praevia. In 2 cases uterine fibroids were later discovered and in another case hydramnios was present. One case was a transverse lie at 28 weeks. In the cases which were subsequently "confirmed" it was noted that there had been no radiological doubt in making the diagnosis.

It was noted that during the years under review a number of cases of placenta praevia had been X-rayed in the antenatal period for

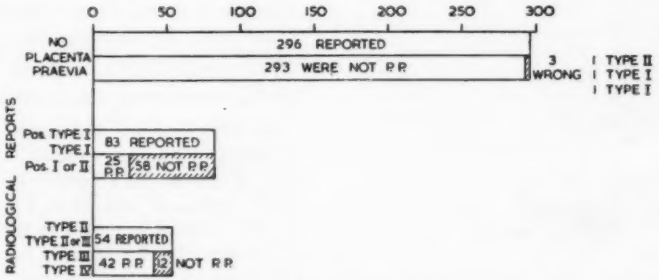

FIG. 4

A clinical follow-up of 433 cases X-rayed for placental site.

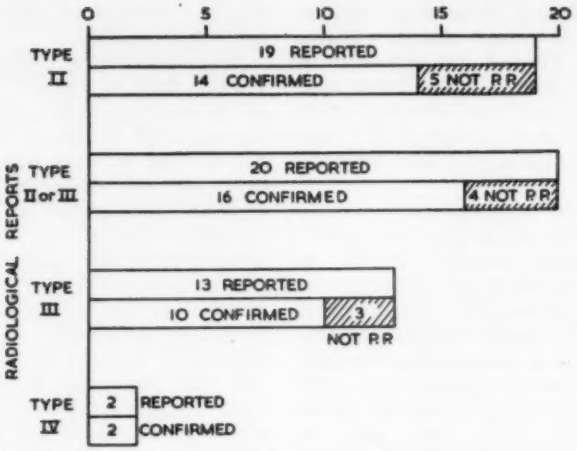

FIG. 5

Clinical follow-up of 54 cases reported Type II, III or IV placenta praevia.

indications other than ante-partum haemorrhage such as maturity, presentation, multiplicity or pelvimetry. It is of interest to record in how many of these cases the abnormal placental situation had been observed in the radiological examination. From Figure 6 it will be seen that in 1950 there were 9 such cases of placenta praevia and in none of these had the possibility of placenta praevia been reported radiologically. After 1950 the reporting of the apparent placental site in routine radiological examinations was introduced and, as a result, 11 cases of unsuspected placenta praevia were noted. In 1953–1954 5 cases, 3 Type I and 2 Type II posterior, were "missed", possibly through an endeavour to reduce the number of cases incorrectly reported Type I. Figure 6 shows the value of noting the placental site in all routine radiological examinations during the antenatal period and determining the site if placenta praevia is suspected.

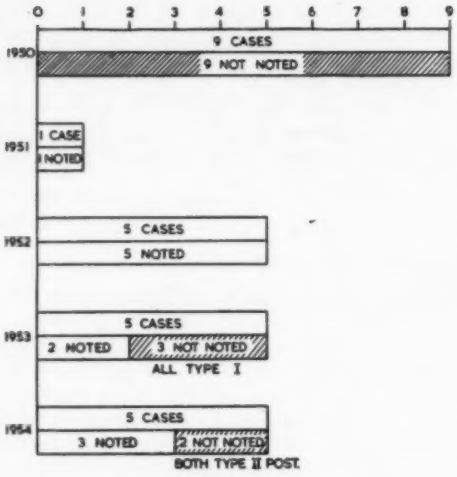

FIG. 6

Cases of placenta praevia discovered on review to have been X-rayed antenatally for reasons other than ante-partum haemorrhage.

THE VALUE OF RADIOLOGY IN PLACENTA PRAEVIA

Radiology is of undoubted importance in excluding placenta praevia, in that many patients who would otherwise be kept in hospital under expectant treatment for a long period, may be allowed to return to their families. This is not only of value socially but saves considerable expense to the hospital service.

The value of establishing the presence of placenta praevia is more difficult to assess as

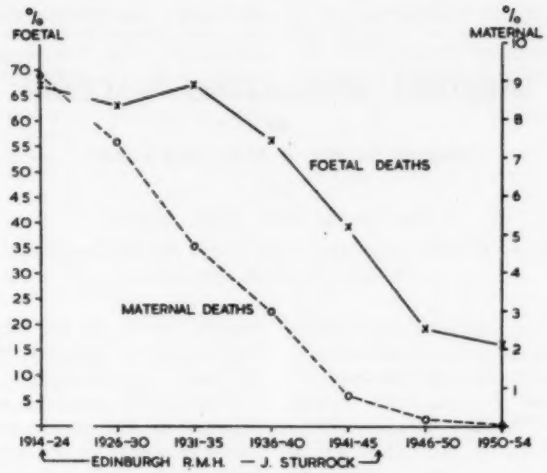

FIG. 7

Maternal and foetal mortality in placenta praevia (S.M.M.P.).

marked improvement in the prognosis for both mother and child had already occurred before the widespread use of X-ray examinations (Fig. 7). Many factors, including better obstetric care, influenced to some extent by radiological examination, improved anaesthesia and blood transfusion have led to a drop in maternal mortality almost to zero and a lowering of the foetal mortality rate to about 15 per cent. However, there may yet be a further reduction in foetal mortality when more widespread use of radiology to define the exact placental site can influence the treatment to be carried out in an individual case (Russell and Warrick, 1955).

SUMMARY

(1) The increased utilization of radiology in the diagnosis of placenta praevia is shown.

(2) Placenta praevia can be diagnosed with accuracy at an estimated duration of pregnancy of 32 weeks or over.

(3) The radiological technique is possible in any general X-ray department and the difficulties associated with interpretation are stated.

(4) The results of a review and follow-up covering a 4-year period are given. These show:

(*a*) Nearly 100 per cent accuracy in excluding placenta praevia.

(*b*) A high degree of accuracy in diagnosing uncomplicated Types II, III or IV placenta praevia.

(*c*) In Type I placenta praevia or in the presence of malpresentation, hydramnios, a small or deformed foetus, fibroid, etc., radiological findings may be uncertain.

(5) The value of looking for the placental site on all routine radiological examinations in obstetrics is emphasized.

ACKNOWLEDGMENTS

We are indebted to the Obstetrical Staff of the Simpson Memorial Maternity Pavilion for allowing us access to the case records and for their helpful advice.

We are especially grateful to Miss West for her help in carrying out the radiographic examinations during the period under review and to Miss Nisbet for her invaluable assistance in preparing the manuscripts.

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UTERINE SARCOMA SIMULATING PLACENTA PRAEVIA

BY

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SARCOMA of the uterus is a rare tumour, and the great rarity of uterine sarcoma associated with pregnancy is indicated by the fact that search of the literature revealed 9 cases only of this association since 1870. Der Brucke (1933) found 3 cases recorded in the preceding 60 years. In the first of these, described by Bernardy in 1885, pregnancy ended in abortion in the fifth month, the patient dying shortly afterwards of secondary spread of the tumour. The diagnosis in this case is open to question, as the tumour was said to be "adenosarcoma". In the second case, reported by Eastman in 1897, a 3-months pregnancy was found to be complicated by fibrosarcoma. Panhysterectomy was performed. The third case, described by Nisot in 1922, was diagnosed during the fourth month of pregnancy. Sarcomatous change had occurred in a pedunculated fibroid. Subtotal hysterectomy was performed. The final outcome of the second and third cases is not recorded.

To these, Der Brucke (1933) added a fourth case, in which myosarcoma was found in a pedunculated uterine fibroid, which had undergone torsion, and had been removed by myomectomy during the fourth month of pregnancy. Five months later, spontaneous vertex delivery of a normal child occurred. Postnatal examination of the mother revealed no abnormality. Hesseltine (1930) records a case of endometrial sarcoma, diagnosed on the nineteenth day of the puerperium. Panhysterectomy was performed, and a course of deep X-ray therapy was administered. The patient was well 7 months later. A case of uterine sarcoma, in which the presenting symptom was uterine bleeding in the fifth month of pregnancy, was described by Rochat (1937). At the time of writing of his case report it had not been decided what treatment was required.

Muret (1937) observed uterine sarcoma in a pregnant diabetic patient. Operation was carried out—the details are not noted—and deep X-ray therapy was given. The patient survived for "several months". Igna and Mitchell (1943) encountered 2 cases within a year. In the first of these, a uterine fibroid 10 cm. in diameter, lying between the layers of the right broad ligament, was removed by myomectomy at the sixteenth week of pregnancy. Histological examination revealed "degenerating fibroblastic sarcoma". Elective Caesarean section was performed near term. There was no recurrence of the sarcoma 2 months after delivery. Their second patient aborted during the fifth month of pregnancy, the placenta being retained. A fibroid polyp measuring $8 \times 7 \times 6$ cm. was removed from the uterine cavity. Histological examination revealed spindle-cell sarcoma. Panhysterectomy was performed. The patient was well 2 months later.

CASE REPORT

We wish to present a further case of uterine sarcoma associated with pregnancy. The patient is a woman of 47 years of age. Between 1945 and 1950, she had 4 pregnancies. The second terminated in abortion at 12 weeks: the other 3 proceeded normally to term, each ending in spontaneous vertex delivery of a healthy mature child. She had had no important illnesses.

She first attended the antenatal clinic at the Southern General Hospital in the twenty-sixth week of her fifth pregnancy. Apart from a mild hypertension—the blood pressure being 142/78 mm. of mercury—no obstetric abnormality was found, although it was noted that definition of the foetus was difficult. This was attributed to her obesity. Because of her age, mild hypertension,

obesity, and rather poor general physique, arrangements were made for her to be delivered in hospital. Subsequent blood pressure levels were normal, and the patient's condition appeared to be satisfactory until the thirty-third week. At that time, it was found to be impossible to diagnose the foetal presentation by abdominal and pelvic examination. X-ray of the abdomen was performed. The report was: "The foetus is lying high in the abdomen, and is almost transverse; maturity about 32 to 33 weeks." Three days later the patient attended again, and reported that she had noticed "a spot of blood" on her underclothing that morning. The presence of placenta praevia was suspected, and she was admitted to the antenatal ward forthwith. Soft-tissue radiography was performed, and anterior placenta praevia diagnosed.

Nine days after the patient's admission to hospital, very slight vaginal bleeding occurred, and this recurred daily. There was no pain, and no vaginal discharge. The foetal position continued to be unstable, usually being transverse. When the patient had been in hospital for 3 weeks—that is, during the thirty-seventh week of pregnancy—there was a sharp rise in her blood pressure to 150/100 mm. of mercury, and slight ankle oedema appeared. On the following day, the 17th February, 1956, there was a rather brisk, painless, vaginal haemorrhage. Therefore, it was decided to examine the patient under anaesthesia without further delay.

Under anaesthesia, examination revealed that the cervix was taken up partially, and was dilated to 2 finger-breadths. Tissue palpably indistinguishable from placental tissue overlay the internal os, the presenting part was free above the pelvic brim, and examination provoked bleeding, about 2 to 3 fluid ounces of bright red blood being lost. The diagnosis of placenta praevia thus seemed to be established. Laparotomy was performed. The lower uterine segment was unusually long for the stage of pregnancy, and large veins coursed over its surface. When the uterus was opened, by a transverse lower segment incision, the lower segment was found to be occupied by a very necrotic tumour, which extended into the upper segment posteriorly. No penetration of the uterine wall by the tumour was seen, and no extra-uterine lesion was found. The foetus, a healthy male weighing 5 pounds 5 ounces, lay transversely, with the head to the left. A normal placenta was implanted anteriorly in the upper uterine segment. At first sight, it was thought that the tumour probably was a sarcoma, arising in a fibromyoma, but that it might be a very necrotic fibromyoma. It was considered that, in either case, no attempt should be made to deal with the condition at that time. While the foetus and placenta were being delivered, a large handful of mushy tumour tissue became detached, and was preserved for histological examination. The lower uterine segment and abdominal wall were then closed. Unfortunately, it was not possible to be certain that every fragment of tumour had been retrieved from the peritoneal cavity.

Convalescence from this operation was uneventful. Histological examination of the tumour tissue showed it to be a leiomyosarcoma. Intravenous pyelography, and X-ray examination of the chest, long bones, spine, and pelvis revealed no metastases. On the 28th February, 1956, the eleventh postnatal day, total hysterectomy and bilateral salpingo-oöphorectomy were performed. The uterus was regular in outline, and measured 16 cm. by 12 cm. by 12 cm. There was no macroscopic extra-uterine lesion.

The immediate post-operative period was satisfactory. The patient remained in hospital until the 25th post-operative day, by which time the abdominal wound was able to withstand X-ray therapy. She was transferred then to the Royal Beatson Memorial Hospital, where a course of X-ray therapy was administered to the lower abdomen and pelvis. She was discharged to her home on the 21st April, 1956, 53 days after total hysterectomy and bilateral salpingo-oöphorectomy had been performed.

When the patient reported to the follow-up clinic on the 17th May, 1956, she was well, and there was no evidence of recurrence of the tumour. Six days later, however, the patient returned, complaining of a small swelling near the mid-point of the abdominal wound. The characteristics of this swelling, which was purplish in colour, tense, and slightly tender, suggested that it was a secondary tumour.

Two days later, on the 25th May, 1956, examination under anaesthesia revealed 2 visible secondary tumours, close together, on the right side of the middle third of the wound, each half an inch in diameter. Both lay just under the skin surface, which was unbroken, and neither extended down to the underlying anterior rectus abdominis sheath. They were included in a wide elliptical incision, and excised. No other secondary tumours were found in the wound or elsewhere. The histological appearances of the excised tissue are described below.

At the moment of writing the patient is still in hospital. The abdominal wound is healing normally, and her general health is satisfactory. However, it is considered that the prognosis is very poor.

Pathological Findings

Tissue from Uterine Cavity on 7th February, 1956

The material consists of 75 g. of friable greyish tissue. Microscopically this is a cellular anaplastic tumour exhibiting numerous giant cells and frequent mitotic figures (Fig. 1). Thin-walled blood vessels are abundant, but connective tissue stroma is minimal; extensive areas of necrosis are included. The general features are those of sarcoma; no cross-striations are revealed by special staining and the condition is regarded as a leiomyosarcoma.

Uterus Removed by Hysterectomy on 28th February, 1956

The specimen consists of a uterus measuring $16 \times 12 \times 12$ cm. which shows a recent operation

wound in the anterior lower segment wall. On sagittal section a large necrotic "fibroid" measuring approximately 12×8×8 cm. is seen to arise from the posterior wall, largely from the lower uterine segment (Fig. 2). Histological examination confirms the presence of a leiomyoma which shows marked hyaline degeneration and extensive necrosis. Figure 3 shows a typical portion of the leiomyoma merging into a more cellular anaplastic tumour. This is seen at a higher magnification in Figure 4 which shows frequent mitotic figures.

Tissue from Site of Previous Scar Removed on 25th May, 1956

In the subcutaneous tissue are seen two well circumscribed nodules of tumour tissue which histologically are secondary deposits of an anaplastic sarcoma containing numerous giant cells and exhibiting frequent mitoses (Fig. 5).

Discussion

The interest in this case is two-fold: the rarity of the combination of uterine sarcoma and pregnancy, and the exactness with which placenta praevia was simulated. The first of these points has been dealt with above. The unstable foetal presentation, slight repeated painless bleeding from the vagina, followed by a more profuse haemorrhage, difficulty in identifying the foetal lie by abdominal examination, and the X-ray appearances, all pointed to a diagnosis of placenta praevia; and that diagnosis appeared to be confirmed by the findings when the patient was examined under anaesthesia. It should be pointed out that X-ray examination indicated correctly that a soft-tissue mass lay in the lower uterine segment. So far as we can discover, this simulation of placenta praevia by a uterine sarcoma is unique.

Summary

Nine cases of uterine sarcoma associated with pregnancy, recorded since 1870, are reviewed briefly. The case report of a tenth patient is presented, and the pathology is described. The rarity of the association, and the manner in which the tumour in the present case simulated placenta praevia, is commented upon.

Acknowledgment

We wish to thank Dr. A. M. Sutherland for his permission to publish this case report, the patient having been treated in his Unit.

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FIG. 2

Sagittal section of uterus removed at hysterectomy showing tumour arising from posterior wall. Previous section incision indicated by arrow. (½ natural size.)

FIG. 1

Anaplastic sarcoma showing giant cells and a mitotic figure. H. & E. ×400.

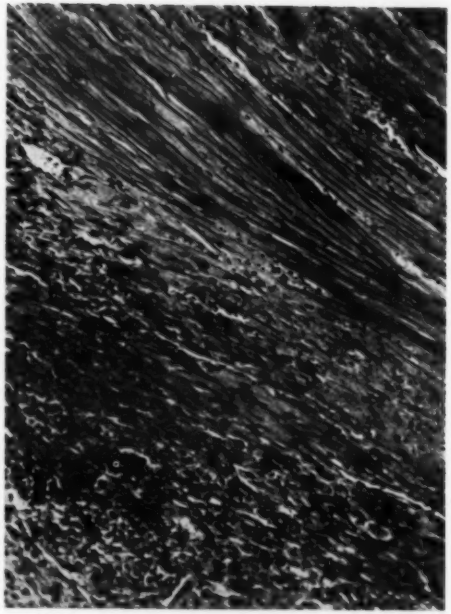

FIG. 3
Typical leiomyoma above merging into cellular sarcoma below. H. & E. ×100.

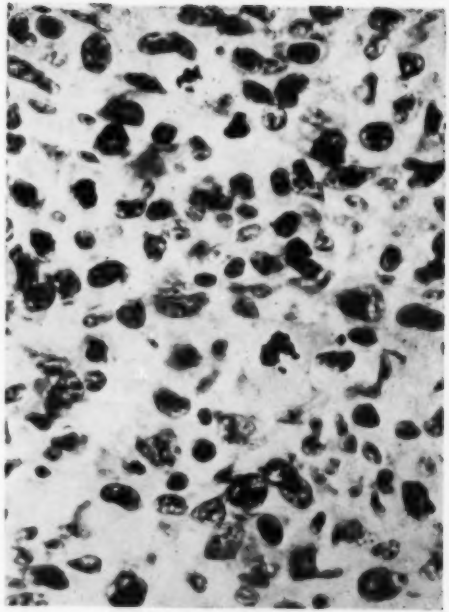

FIG. 4
Leiomyosarcoma showing frequent mitoses. H. & E. ×400.

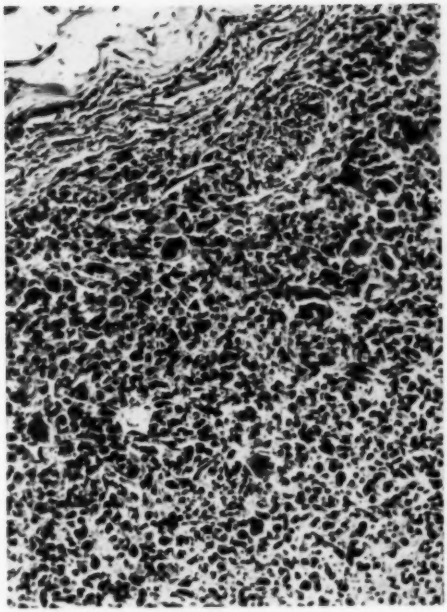

FIG. 5

Secondary leiomyosarcoma in subcutaneous tissue. H. & E. ×100.

MIXED MESENCHYMAL TUMOUR OF THE UTERUS WITH SUPERIMPOSED ADENOCARCINOMA

Case Report

BY

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THE mixed mesenchymal tumours of the uterus are rare and both Novak (1952) and Faulkner (1952) consider that each case should be reported. Several authors have reviewed the literature and have added cases of their own. Glass and Goldsmith (1941) found 95 cases. Hardy and Moragues (1952) reported a total of 21 further cases. Other cases have been reported by Shapiro (1931), McElin and Davis (1952), Chesky, Dreese and Hellwig (1952), Allen (1953), McCutcheon, McDonald and Piven (1953), Wilson, Graham, Thornton and Nokes (1953), Bickel and Bennett (1954), Sternberg, Clark and Smith (1954), Laufe and Meyers (1954), Symmonds and Dockerty (1955).

CASE REPORT

Mrs. E.G., aged 72 years, was admitted to hospital on 16th August, 1955. She had been bleeding from the vagina intermittently for 2 years and continuously for 4 months. Some weeks before admission she had had a heavier blood-loss lasting several minutes. The menopause had occurred at the age of 50. Up to that time her menstrual cycle had been regular with 4 days blood-loss every 30 days.

Her bowels were open daily and micturition was normal apart from slight stress incontinence. She had been gaining in weight for some time. She had not had any pills or medicines for the 4 years prior to her admission. She had had 1 previous pregnancy 42 years ago. The pregnancy, labour and lying-in periods were normal.

In 1945 she had had a slight cerebral vascular accident but there was no residual paralysis.

When examined she was an obese woman with a high colour. The cardiovascular and respiratory systems were normal. The blood pressure was 140/80 mm. Hg. The abdomen was normal.

Vaginal examination was impossible. The vulva showed senile changes, and the vaginal introitus just admitted a finger tip. Rectal examination was inconclusive. On 19th August, 1955, examination under anaesthesia was carried out. The vagina admitted 1 finger. Two stenosing bands were found and these obscured observation of the cervix and palpation of the uterus and appendages. Rectal examination appeared to reveal a bulky and soft uterus. Although senile vaginitis was present, this was not considered to be of such a degree as to produce this quantity of bleeding and a provisional diagnosis of carcinoma of the body of the uterus was made.

At laparotomy, the uterus was found to be of normal size. The ovaries were atrophic. The left ovary was adherent to the pelvic colon and to the lateral wall of the pelvis. There were no palpable glands. A total hysterectomy and bilateral salpingo-oöpherectomy were performed. As the uterus was being removed from the vagina a small piece of soft tissue was extruded from the cervical canal which could not be closed pre-operatively owing to the presence of the occlusive vaginitis.

The patient's post-operative convalescence was delayed by the appearance of a haematoma of the wound, but this discharged itself and healing was then rapid. She was discharged on the 27th September. She was admitted to Hammersmith Hospital on 14th October, 1955, and a course of deep X-ray therapy was given.

PATHOLOGICAL EXAMINATION

Gross Appearance

The specimen consisted of the uterus with both appendages. The serosa was smooth and greyish-brown in colour with some haemorrhagic areas. The vaginal portion of the cervix was covered by a smooth grey epithelium. Section of the uterus showed the cavity to be occupied by a mass of firm, grey, crumbling growth and blood clot infiltrating the muscular wall of the uterus to within 0·5 cm. of the serosa at the fundus. The growth appeared to be arising from the fundus of the uterus. Cut section of growth showed very hard, possibly calcified areas in some places. The cervical canal was lined by smooth grey mucosa. Both ovaries were normal externally and on section. The fimbrial ends of both tubes were patent.

Microscopical Appearance

A very well-differentiated tubular columnar celled carcinoma of the body of the uterus (Fig. 1). The polypoidal portion of the growth was highly cellular and contained hyaline cartilage (Fig. 2), osteoid tissue and calcified bone (Fig. 3). Myxomatous tissue was also present (Fig. 4).

Striated muscle cells or primitive cells, rhabdomyoblasts, were not found. The tumour was considered to be a mixed mesenchymal tumour of the uterus with an associated adenocarcinoma of the endometrium.

Discussion

The mixed mesenchymal tumours fall into 2 types:

(1) Pedunculated tumours of the cervix occurring in young children—the botryoid tumour.

(2) Identical growths of the body of the uterus occurring in women after the menopause.

These tumours originate from cells which are not normally present in the uterus. These cells are solely of mesodermal origin and the tumours, therefore, are unlike the teratomas, the components of which are derived from the three germinal layers. This group of tumours resembles the Wilms tumour of the kidney and the mixed parotid tumour, both of which have been reported in considerable numbers.

Description of the tumours of this group is confused by a multiplicity of terms used to describe tumours of mesodermal origin found in the uterus. McFarland (1935) found 119 terms in the literature describing these cases. It would appear that the dominance of one type of tissue over others has been the source of this lengthy nomenclature. The criteria for the inclusion of different tumours in the category of mixed mesenchymal tumours have been discussed at length by Läwen (1905), Meikle (1936), Lebowich and Ehrlich (1942) and Ehrlich (1942). Most authors (Ferreira, 1951; Hardy and Moragues, 1952; Symmonds and Dockerty, 1955, among them) consider that, as these tumours are a clinical entity and follow a typical course, it would be unwise to exclude any tumour which is made up of two or more heterotopic elements and in which one particular type of cell cannot be identified.

The striated muscle cell and the rhabdomyoblast were not present in the sections of the specimen removed here. Nevertheless, the presence of cartilage, osteoid tissue and myxomatous tissue is sufficient to establish the diagnosis.

Novak (1952) has pointed out the occasional appearance of epithelial as well as connective tissues within these tumours. Furthermore, the epithelial elements may appear as adenocarcinoma. This represents a carcinosarcoma in the strictest sense as opposed to the "collision" tumours of Meyer or the "combination" tumours where there is a mere co-existence of carcinoma and sarcoma. Figure 3 shows the epithelial and connective tissue elements in the same field.

The histogenesis of these tumours is still in doubt—the three prevalent theories are those of Pfannenstiehl, Wilms and Lahm.

Pfannenstiehl (1892) considered that the different types of tissue found in these tumours derive from a metaplasia of normal connective tissue of the uterine mucosa. Nicholson (1918) and Willis (1948) adhere to this theory which does not explain the appearance of striated muscle cells in about half of the cases reported. In the opinion of Altmann and Rosenthal (1952), too, metaplastic chondroid cartilage does not have the appearance of the normal cartilage described in their case and identical with that seen in the case reported herein.

Wilms (1899) believed that the origin of these tumours was from cells carried down by the Wolffian duct. Novak (1947) considers that this theory is more plausible than that of Lahm (1928) and Meyer (1930) who considered that the mesodermal cells originated from Müllerian rests. Sternberg, Clark and Smith (1954) point out that the majority of the tumours occur at the uterine fundus, i.e., above the entrance of the Wolffian duct in the broad ligament and that this fact is more in favour of the Müllerian cell rest theory. Whatever theory is held, Willis's observation of the apparent absurdity of the theory of cells resting in the uterus for periods of 50, 60 or 70 years before becoming active, is provoking.

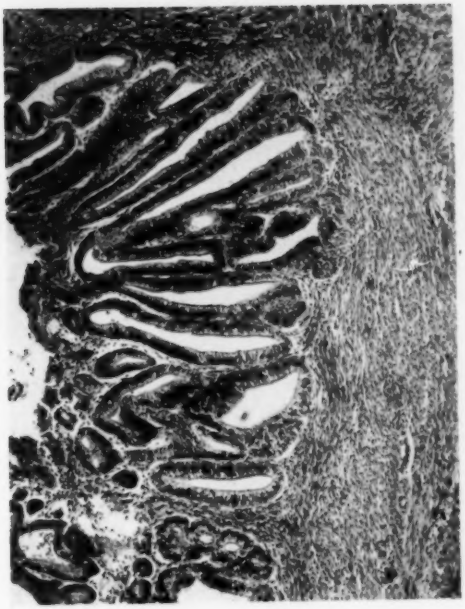

FIG. 1

Well-differentiated adenocarcinoma of the endometrium. H. & E. × 65.

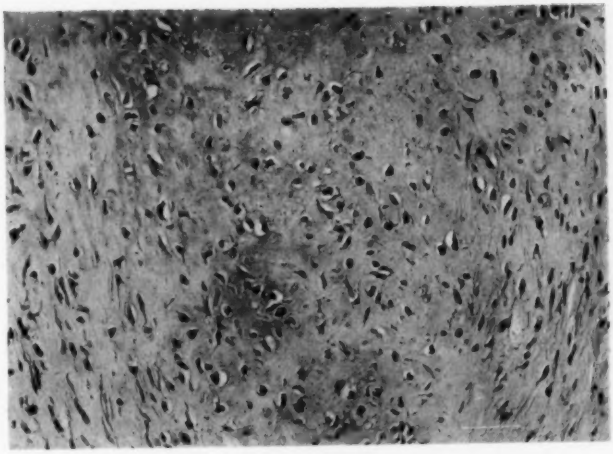

FIG. 2

Section of the tumour showing well-formed hyaline cartilage. H. & E. × 135.

FIG. 3

Section of the tumour showing osteoid tissue, calcified bone and epithelial elements. H. & E. × 50.

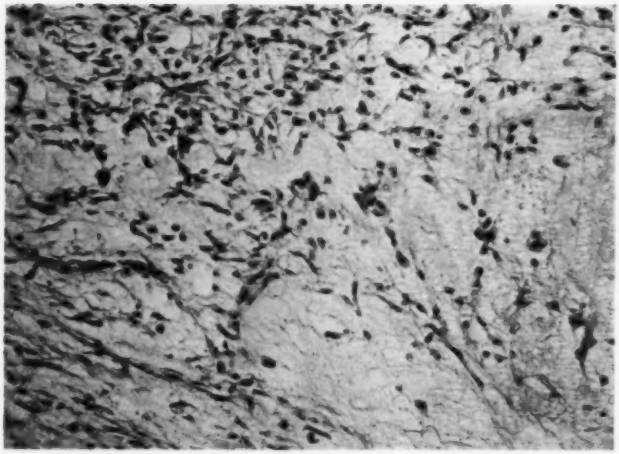

FIG. 4

A portion of the tumour containing well-formed myxomatous tissue. H. & E. × 135.

G.W.K.

The clinical progress of these tumours is disheartening. All authors report a very poor prognosis for this type of growth, local spread and distant metastases occurring within a few weeks to months of the appearance of the first symptoms. Only isolated cases of apparent cures have been reported.

The minimum treatment is removal of the uterus and appendages and this should be followed by a course of deep X-ray therapy although the efficacy of this is in doubt since blood-borne metastases are the commonest cause of failure (Way, 1951).

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DYSTOCIA DUE TO FOETAL ASCITES

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OBSTRUCTED labour resulting from foetal abdominal swelling is an extremely rare occurrence. Such abdominal enlargement may result from neoplasm, dilated bladder, congenitally cystic kidneys, hydrops foetalis, or idiopathic ascites.

The foetal abnormality is usually discovered following delivery of the head and shoulders when further progress is arrested (Shaw and Marriott, 1949; Beacham and Beacham, 1952). It would appear, however, that the diagnosis can be made before labour with considerable certainty by radiography. Puig y Roig (1948) reported 1 case of foetal ascites thus diagnosed, and 3 cases suspected, all confirmed at delivery.

In the following case the ante-partum X-ray plate clearly demonstrated deformity of the foetus due to gross abdominal enlargement (Fig. 1).

A gravida-6, aged 27, was admitted to the hospital at the thirty-sixth week of pregnancy. She had attended a local authority antenatal clinic on only two occasions, and there she was noted to be "big for her dates", but an X-ray was reported as showing a single foetus. She had been well throughout her pregnancy apart from slight swelling of the ankles.

On admission the patient complained of irregular abdominal discomfort. The uterus was enlarged beyond the size of a normal full-time pregnancy, the abdominal girth being 42 inches. A fluid thrill was present, and a single foetus could be made out presenting by the head. The presenting part was high and free. The foetal heart was heard to the right and below the umbilicus.

In view of the obvious hydramnios, X-ray of the abdomen was carried out, but, before the films could be examined, the patient went into labour. When the membranes ruptured spontaneously vaginal examination revealed the vertex at the level of high cavity in the right occipito-anterior position. The cervix was half dilated.

Labour progressed satisfactorily, the first stage lasting 5 hours. The head was delivered without difficulty, but there was delay in the birth of the shoulders. Both arms were brought down. No further progress was possible despite fundal pressure and arm traction. The foetal heart was no longer heard. The patient was anaesthetized and a hand was introduced along the ventral aspect of the foetus. The foetal abdomen was felt to be grossly distended although apparently quite soft unless traction was made on the head and arms.

Delivery could not be effected, and a Simpson's perforator was introduced and the point pushed through the foetal abdominal skin in the epigastric region. A finger was introduced into this opening and was easily pushed into the foetal abdominal cavity.

When the finger was removed a large quantity of clear straw-coloured fluid escaped from the vagina. At least one litre of fluid was evacuated aided by gentle traction on the foetal head and arms. The body of the infant then escaped without difficulty. The placenta was expressed, the patient given 0·25 mg. ergometrine intravenously, and the uterus and vagina were carefully explored. No damage to the maternal soft tissues was detected, and the third stage blood loss was minimal. The placenta, which weighed 1 pound 4 ounces, showed no gross or microscopical abnormality.

The puerperium was uneventful.

The infant (Fig. 2) was a 7 pounds 4 ounces stillborn male, and the grossly distended abdomen contained a further 500 ml. of fluid. Post-mortem examination revealed no abnormality other than the ascites and slight hepatic autolysis.

The patient's Wassermann reaction was negative, and her blood group "O", Rh positive. A specimen of blood submitted to the Regional

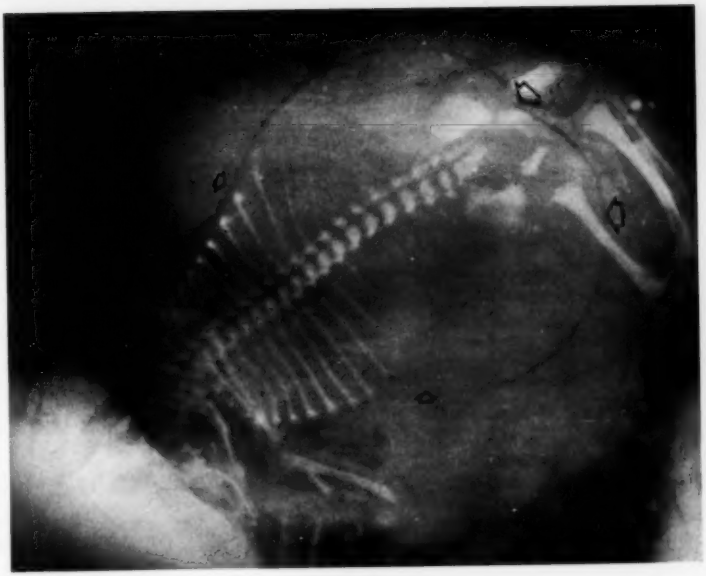

FIG. 1

X-ray showing obviously abnormal foetus and outline of abdominal swelling.

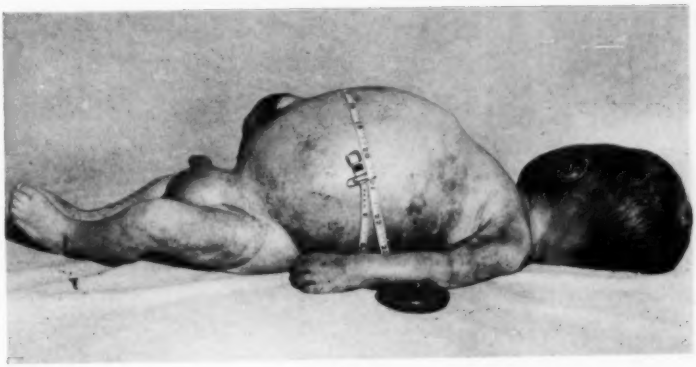

FIG. 2

Foetus with abdomen refilled with an amount of fluid equivalent to that drained at paracentesis.

Blood Transfusion Centre revealed no unusual antibodies.

Discussion

Owing to the relative softness of the foetal abdominal swelling it was necessary to perform paracentesis with a sharp pointed instrument, and the Simpson's perforator was found to answer this purpose. Mayo's scissors were used by Beacham and Beacham for the perforation in the case described by them.

DeLee and Greenhill (1947) suggest resection of several foetal ribs and the sternum, followed by perforation of the diaphragm to evacuate the abdominal contents, but it is unlikely that this more major procedure need ever be employed except for solid tumours.

Acknowledgments

We wish to thank Dr. D. McKay Hart, Director of the Department of Obstetrics, Stobhill General Hospital, for permission to publish, and also Mr. P. Waldie, of the Department of Photography, for his assistance.

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CONGENITAL SYPHILIS
CONFUSION WITH ERYTHROBLASTOSIS FOETALIS

BY

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CONGENITAL syphilis today is not a common condition, and with thorough antenatal care should be extremely rare. There were 191, 372, 110, and 67 cases of congenital syphilis under one year in the Ministry of Health (England and Wales) returns for the years 1940, 1948, 1952, and 1954 respectively.

Its relative rarity, however, imposes dangers on the patient by reason of the difficulties which occasionally arise in its diagnosis. Certainly congenital syphilis and erythroblastosis foetalis may be difficult to distinguish (Gilmour, 1944). The syphilitic placenta is described as large, pale and of greasy appearance, and the placenta in erythroblastosis foetalis is large, pale and oedematous in the typical case of this disorder (Barnes, 1948). Although there may be a histological resemblance in the enlarged villi and diminished vascularity which occurs in the placenta in either disease, in congenital syphilis there is an endarteritis and fibrosis, and in erythroblastosis there occurs oedema and persistence of the Langhans' layer (Henderson, 1942; Barnes, 1948). Both conditions moreover may result in hydrops foetalis or icterus gravis neonatorum (Nabarro, 1954; Gilmour, 1944).

The following case is one in which confusion between these two disorders remained unresolved for an unusual length of time.

The case is that of a congenital syphilitic mother who gave birth, on two occasions, to macerated foetuses, which, if they had survived, would have been examples of second generation congenital, or third generation, syphilis.

The question of third generation syphilis has been discussed by Nabarro (1954), and the postulates of Fournier (1905) and Finger (1900) must be remembered. The modern concepts of immunity and allergy in syphilis have been thoroughly reviewed by Urbach and Beerman (1947).

In February, 1949, the patient, aged 28 years, was delivered of a 34-weeks macerated foetus. The patient was noted to be Rhesus positive and the Kahn reaction was negative. At post-mortem the macerated foetus and placenta showed the "usual post-mortem changes of this condition. There were no congenital or gross lesions. The organs were gelatinous, and cavities filled with altered, haemolysed blood." There was no report on histology, and no firm diagnosis was made.

In January, 1950 the patient was again delivered of a 32-weeks macerated foetus, having sustained a severe hydramnios at 31 weeks. She was again grouped Rhesus positive, group O, and the serum tests for syphilis (WR and Kahn) when performed during the puerperium were strongly positive. At post-mortem the "appearances were consistent with erythroblastosis foetalis". There was no report on histology.

The patient's condition was reviewed at this hospital where she was sent in February, 1950 when the serum tests for syphilis were returned positive. Her mother, aged 57 years, was found to have no evidence of syphilis. Similarly, her husband had neither historical, physical, nor laboratory evidence of syphilis. The patient's father and 3 of her brothers were alive and well, but were not examined (by the request of the patient). One other brother had died when young.

There was no evidence pointing to syphilis in the patient's personal history, and there was said never to have been extra-marital sexual contact. The specific serum tests were verified as being

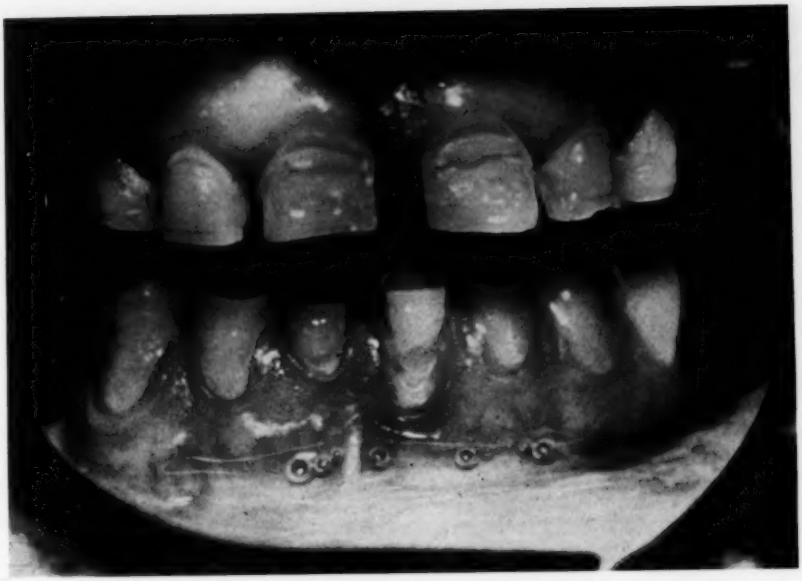

FIG. 1

Shows peg-shaped upper central incisor teeth.

strongly positive. The relevant physical signs were: leucoderma of the left thigh, markedly peg-shaped upper central incisors (Fig. 1) and a mildly congenital syphilitic facies. The C.S.F. was normal. The patient had received no specific therapy. She then was treated and remained under observation. In January, 1951 typical pigmented scars of old congenital syphilitic choroiditis were noted in both fundi. In January, 1953 the patient had an attack of interstitial keratitis with vision deteriorating in that eye to 6/18.

The patient's specific serum tests have remained strongly positive. In September, 1952 the patient gave birth to a healthy male child whose serum tests for syphilis were temporarily positive. In February, 1955 she gave birth to a second healthy infant whose serum tests have been negative. No Rhesus antibodies were detected in the patient's serum.

Conclusion

This patient was at one time (prior to February, 1950) diagnosed as a possible case of Rhesus blood group incompatibility, in spite of the laboratory findings and the obstetric history, both of which made it extremely unlikely. Had a second Kahn or Wassermann test been performed, or the results of histological study been available, it is doubtful whether such a diagnosis could have been entertained. The fact that the patient had a suggestive congenital syphilitic facies and incisor teeth formation, far from being a help, might have confused the issue by leading one to believe that the patient's syphilis, being of the congenital variety, would be an unlikely source of the obstetric disorder.

I am indebted to Dr. J. Morton of Guy's Hospital, whose patient this is, for allowing me to publish the details of her case.

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A CASE OF PLACENTA PRAEVIA COMPLICATED BY AFIBRINOGENAEMIA

BY

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IN view of the interest shown in the occurrence of afibrinogenaemia in pregnancy, and as there does not appear to be a reference in the British literature associating this complication with placenta praevia, the following case record is reported.

Mrs. E.W., a secundigravida aged 32, was admitted to hospital because of a sudden painless ante-partum haemorrhage of about half a pint. The pregnancy was of 34-weeks duration. Her first pregnancy, 4 years previously, had resulted in the spontaneous delivery of a live male infant at term.

On admission the patient's general condition was good, the blood pressure was 120/80 mm. Hg and a catheter specimen of urine contained no albumen. The foetus was lying transversely, the foetal heart rate was regular and there was no uterine tenderness.

On the morning following admission one pint of whole blood was transfused as the haemoglobin was 9·7 grams per cent.

The patient remained in hospital and no further bleeding occurred until the thirty-eighth week of pregnancy. Profuse bleeding commenced in the early hours of morning of the day chosen for examination under anaesthesia. An intravenous drip was commenced immediately with normal saline solution, and at this stage the patient's pulse rate was 90/min. and the blood pressure was 140/90 mm. Hg. Twenty minutes later, at the onset of anaesthesia, the patient was collapsed and the blood pressure had fallen to 100/70 mm. Hg. Blood transfusion was commenced, a lower segment Caesarean section was performed and a live female infant was extracted without difficulty. The placenta was attached to the posterior lower uterine surface and also extended to cover the internal cervical os completely. There was profuse bleeding during the early part of the operation but haemostasis was effected without undue difficulty and blood clots were forming normally. At the termination of the operation the blood pressure was 90/60 mm. Hg. Two pints of blood had already been transfused and transfusion was maintained with Dextran whilst more blood was crossmatched. The clinical estimate of the patient's blood loss was 4 pints. During the next hour there was steady improvement and the blood pressure slowly rose to 110/70 mm. Hg. Then, suddenly, profuse vaginal bleeding occurred. Ergometrine 0·25 mg. was given intravenously and the same dose was also given intramuscularly and the bleeding was arrested. The measured loss was one pint. Ten minutes later vaginal bleeding recommenced and it was also noted that the abdominal dressing was soaked with blood. On removal of the dressing blood was seen to be spurting from the centre of the wound. The clips and sutures were removed from this area but no single bleeding point was seen. The wound surfaces were just oozing blood freely. Under local anaesthesia six silk sutures were inserted into the skin and tied firmly over a large gauze roll. This arrested the haemorrhage from the abdominal wound but a trickle of blood continued to emerge from the vagina. By this time the pulse rate had risen to 132 per minute and the blood pressure was 84/50 mm. Hg. Neither ergometrine nor intravenous pitocin had any effect in controlling the bleeding. Blood transfusion was just maintaining the patient's poor general condition.

At the onset of bleeding after the operation 20 ml. of blood had been taken from the patient in order to have a reserve supply of serum. It

was noted that one hour after the collection of this blood no clot had formed. The clotting time was in fact in excess of 12 hours as by that time the blood had been used for laboratory investigation. The plasma fibrinogen level was later reported to be 90 mg. per cent. (Normal 250 mg. –350 mg. per cent.)

In view of the continued oozing and the failure of clot formation a presumptive diagnosis of acquired afibrinogenaemia was made. The following quick tests were performed, protamine sulphate, tested active solutions of thrombin and human fibrinogen were added in turn to separate specimens of the patient's unclotted blood. Only the addition of human fibrinogen resulted in the formation of a firm clot. (Two minutes.) This finding supported the presumptive diagnosis and arrangements were made for the supply of whole blood and human fibrinogen. By this time a total of 10 pints (6 litres) of stored whole blood and one pint of Dextran had been transfused and the clotting time was 10 minutes (Lee and White) though only a poor clot was formed. An intravenous injection of 420 mg. of human fibrinogen brought the clotting time down to 3 minutes. A further 1,008 mg. of human fibrinogen and 6 pints of blood (3,500 ml.) were given, 4 pints (2,300 ml.) of blood being fresh donor's blood. Bleeding had ceased after the first injection of fibrinogen and the plasma fibrinogen level was later reported as being within normal limits.

The extent of intra-peritoneal bleeding was difficult to decide, but fullness and tenderness in the flanks persisted for 7 days. The patient made a slow recovery. The urinary output steadily increased after the initial oliguria whilst hypotension existed, and partial breast feeding was also accomplished. A *Bacterium coli* urinary infection responded to a course of streptomycin. A deep calf vein thrombosis developed on the 11th post-operative day and this was treated with intramuscular heparin. Wound healing was delayed by infection and the lower half of the wound healed by secondary intention. The patient was discharged from hospital 7 weeks after her operation fit and well. The abdominal scar was unsightly and pelvic examination revealed a normally involuted, mobile anteverted uterus.

Discussion

In 1901 De Lee mentioned a haemophilic tendency in a case of "utero-placental apoplexy". Since that time many cases of prolonged bleeding due to a reduced plasma fibrinogen level have been described in association with accidental haemorrhage, amniotic fluid emboli and in cases of intra-uterine death of the foetus associated with Rhesus immunization. In 1919 Obata found that the infusion of placental extracts into mice caused blood defibrination and Sakurai (1929) confirmed this finding in dogs. Howell (1941) found that, in dogs, rapid injection of thromboplastin caused extreme intravascular clotting and death of the animal whereas sub-lethal doses produced defibrination. Schneider (1947) concluded, after extensive experiments in dogs, that thromboplastin was the toxic element contained in placental extracts which when liberated in the blood stream resulted in afibrinogenaemia. Page, Fulton and Glendenning (1951) showed that the injection of placental extracts caused a fall in the plasma fibrinogen level and that the critical level for bleeding was 200 mg. per cent.

Weiner and his colleagues (1950, 1953) studied several hundred cases of abortion, hydatidiform mole, placenta praevia and "premature separation of the placenta" and found that the plasma fibrinogen level fell after the bleeding in severe degrees of placental separation. They describe 34 cases in which they treated this complication with blood transfusion and intravenous fibrinogen. They do not, however, describe a case of placenta praevia amongst their treated cases.

It is argued that the release of thromboplastin can cause a severe depletion of the circulating fibrinogen, the liver being unable to correct the deficiency in time to prevent severe haemorrhage. Prolonged hypotension may in turn cause liver damage and so adversely affect the ability of the liver to produce fibrinogen. Page and his colleagues also describe that the injection of placental extracts in dogs caused liver necrosis.

The problem remains, however, as to the portal of entry of thromboplastin into the maternal circulation. Weiner postulates that the coagulant containing liquor is forced into the open venous sinusoids at the side of placental separation by the increasing intra-uterine pressure in labour and that the liquor is further

enriched with thromboplastin released from the decidua.

In the case described above, the amniotic cavity was intact. It is, therefore, suggested that massive blood loss alone may be a cause of acquired afibrinogenaemia. The normal plasma fibrinogen level is between 250 mg. to 350 mg. per cent. A loss of six pints of blood will severely deplete the circulating fibrinogen level even though the circulating fluid volume may be nearly normal due to transfusion. Stored blood has little fibrinogen content and Dextran in excess may further disturb the coagulation mechanism. The concurrent shock will impair liver function and so delay restoration of the plasma fibrinogen level above 100 mg. per cent. This figure is believed to be the critical level in the human. In cases of accidental haemorrhage the blood-loss associated with a sudden increase of the circulating thromboplastin level may result in defective coagulation due to defibrination. However, Crichton's (1950) figures show that, in cases of accidental haemorrhage, rupture of the membranes when labour is established as opposed to rupture of the membranes before the onset markedly reduces the maternal mortality. This is in opposition to the results expected if Weiner's postulate is correct. Afibrinogenaemia associated with Rhesus isoimmunization may be the result of defective placental permeability.

Summary

A case of severe haemorrhage due to placenta praevia is described. Recurrence of bleeding was thought to be due to a lack of circulating fibrinogen and treatment consisted of blood transfusion and the available human fibrinogen. Treatment with fresh blood and fibrinogen should be instituted on the result of simple laboratory tests and not delayed until more elaborate investigations can be performed. All cases of severe haemorrhage in pregnancy should have simple clotting tests and such tests as the addition of fibrinogen and thrombin to samples of blood if the clotting time is abnormal. Thirty ml. of blood should be reserved for fibrinogen content examination and electrophoretic patterns.

It is suggested that severe haemorrhage alone even in the absence of thromboplastin release may deplete the circulating plasma fibrinogen level sufficiently to prevent blood coagulation. This is a factor of importance in cases of abortion, placenta praevia and post-partum haemorrhage as the circulating blood volume may be maintained with stored blood and plasma substitutes.

My thanks are due to Mr. O. Lloyd for permission to publish this case report. I am indebted to Dr. J. Marks and Dr. N. R. Lawrie of the John Bonnett Clinical Laboratories, Cambridge, for the laboratory investigations. I should also like to acknowledge the assistance of Dr. J. Walker of the Regional Transfusion Service who organized the supply of fibrinogen and of Group B blood.

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HYGROMA OF THE NECK IN THE FOETUS

Report of a Case

BY

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THIS case is reported because of the extreme rarity of the condition and because of the great difficulty experienced in delivering the child.

CASE REPORT

Mrs. C.S., aged 28, had had 8 previous pregnancies. All her babies had been delivered spontaneously and all weighed in the region of 8 pounds except her first which was delivered prematurely and which weighed only 3 pounds. There had been no abnormalities during her previous pregnancies or confinements and all her children were alive and well.

During this ninth pregnancy the patient had been supervised by her own doctor and had not been booked for hospital delivery. She had remained well and her expected date of confinement was 17th May, 1955. Labour commenced at 8 a.m. on 18th May, 1955 and she had a rather inert first stage, lasting, in all, 11 hours. The membranes ruptured at full dilatation of the cervix and thereafter the patient was allowed to push with each contraction. After two and a half hours, as the foetal head had been showing for some time but all advance had ceased, she was anaesthetized and her doctor applied forceps but, in spite of strong traction, failed to deliver the patient. He came to the conclusion that the head was lying in the occipito-posterior position and, as manual rotation failed, the patient was transferred to the Simpson Memorial Maternity Pavilion.

On admission, her general condition was fairly good, although she was somewhat dehydrated and very tired. Her blood pressure was 116/80 mm. mercury and her pulse rate was 86 per minute. Examination of the abdomen revealed the presence of a very large baby but accurate palpation of the presentation and position was impossible because of the increased tone of the uterus which was contracting strongly every 2 minutes. There was a mid-line suprapubic swelling which was thought to be the distended bladder but which, in retrospect, must have been part of the foetus. The foetal heart was loud and regular, beating at a rate of 140 per minute. Vaginal examination showed the foetal head to be lying in the mid-cavity of the pelvis and when the patient pushed with a contraction, it descended to the introitus. The sagittal suture was lying in the transverse diameter of the pelvis with the occiput on the left side and there was no caput formation and no moulding.

She was anaesthetized with cyclopropane and oxygen and placed in the lithotomy position. Two different catheters were passed with ease into her bladder but only one ounce of concentrated urine was obtained. Examination under anaesthesia confirmed the presentation and position but it was found that the head had receded to the brim of the pelvis and all attempts at manual rotation failed.

The patient obviously had a roomy pelvis and a very deficient perineum with lax vaginal walls so that there was no obvious local cause for the delay. The vault of the skull showed no evidence of hydrocephalus. Further attempts at manual rotation were partially successful and Haig-Ferguson forceps were applied rather obliquely. Initial traction pulled the head down to the outlet but there the forceps slipped from the head which then returned to its previous level. Careful re-examination confirmed that the diagnosis of the presentation and position was correct and the same manœuvres were repeated with precisely the same results. At this point it was thought that the main difficulty was the size of the baby.

Thereafter Kielland's forceps were applied using the wandering blade method, considerable difficulty being experienced in placing the anterior blade in position. Traction produced rotation and descent of the head fairly easily but again the forceps slipped off when the head had reached the outlet. The possibility of a constriction ring was considered but there was no evidence of this from abdominal palpation and an attempt to pass a hand into the uterus failed because of the large size of the head. The anaesthesia was deepened as much as possible and as the patient's pulse rate had risen to 140 per minute and her blood pressure had fallen to 95/60 mm. mercury, an intravenous drip of Dextran was commenced and 2 pints of blood were crossmatched, The foetal heart was still present but it was irregular and the rate had fallen to 100 per minute.

Kielland's forceps were again applied and with strong traction and forced locking of the blades, the head was delivered with great precipitancy. The remainder of the child was easily delivered and the placenta was expressed immediately. Because of the various manipulations

carried out, a hand was passed into the uterus to palpate the lower segment and this was found to be intact. During delivery there had been considerable blood loss from vaginal lacerations and the Dextran was replaced by blood transfusion. The lacerations were then repaired with interrupted catgut sutures and mersilk sutures. In all, the patient was given three-quarters of a pint of Dextran and 2 pints of blood, following which her general condition was satisfactory. She made an uninterrupted recovery and was discharged on the eighth day of the puerperium.

The baby, a male, was stillborn and weighed 11 pounds 14 ounces. There was a symmetrical cystic swelling of the lower face and neck extending from the lower margin of the eyes to the upper border of the manubrium sternii (Fig. 1). The tumour measured 20 cm. from side to side and the distance from the top of the head to the lower margin of the swelling was 23 cm. Cross-section of the tumour showed it to be subdivided into many cysts of varying size which penetrated deeply into the lateral muscles of the neck and also posteriorly. The cysts were lined by a single layer of flat endothelial cells and the diagnosis was one of Cystic Lymphangioma or Hygroma.

According to Potter (1952) these tumours are most often located on one side of the neck but occasionally they may be multiple and may be found in other locations, especially in the axilla. They may be unilocular or multilocular and are not visibly connected with lymphatic channels.

There are few cases mentioned in the literature but those which I have been able to find are of some interest. The patient described by Hendry (1926) was unfortunate in that she had a contracted pelvis of the rachitic type, the true conjugate being $2\frac{3}{4}$ inches. Her first pregnancy was terminated by classical Caesarean section. At term in her second pregnancy the child was noted to be large and to be presenting by the breech and again classical section was performed. Great difficulty was experienced in delivering the head because of a hygroma measuring 17 cm. from side to side and 14 cm. from the lower lip to the lower border of the tumour. In the case reported by Johnstone (1932), the patient, in her third pregnancy, had a labour lasting 24 hours and forceps were applied because of second stage delay. There was great difficulty in promoting extension of the head as it passed through the outlet because of a hygroma of the neck with a circumference of 21 cm. The difficulty at the outlet was similar to that experienced in the case described.

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FIG. 1
Hygroma of neck.

SUPERFICIAL DISSEMINATION OF CANCER OF THE UTERINE BODY. CYTOLOGICAL EXAMINATION OF SMEARS FROM THE TUBES AND THE POUCH OF DOUGLAS

BY

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IT is generally recognized that dissemination from cancer corporis uteri may occur both by the lymphatics and by the blood stream. Dissemination to the ovaries and peritoneum is not rare, and there is a theoretical possibility that this may be the result of superficial dissemination of the tumour cells through the tubes and across open peritoneal surfaces with subsequent implantation and growth.

In order to investigate this possibility smears have been examined from the tubes and washings from the Douglas pouch in cases of cancer corporis uteri. The investigation was made on the suggestion of Dr. Thor Dahle, chief of the Gynaecology Department of the Norwegian Radium Hospital, whence the material has been obtained.

MATERIAL, METHODS AND TECHNIQUE

The preparations were obtained from 27 patients on whom exstirpatio uteri et adnexorum had been performed. One patient was 36 years old, the others were from 48 to 79 years old. The material consists of:

25 adenocarcinoma corporis uteri;
1 sarcoma corporis uteri;
1 adenocarcinoma in the right tube with metastases to the corporis uteri.

In all cases the diagnosis has been histologically verified by microscopy from the uterus, tubes and ovaries.

Macroscopic examination of the uterus in the 25 cases of adenocarcinoma corporis uteri revealed that in 10 cases the walls of the entire uterus were lined with tumour tissue, in 12 cases the tumour was localized to the anterior or posterior wall and was from bean to egg size. In 3 cases no tumour was demonstrable macroscopically but the mucous membrane was roughened and there were small polyps. In some cases the tumour infiltrated the myometrium but never penetrated the wall completely. The intact portion of the myometrium measured from the serosa side was 0·3–2 cm.

In the one case of sarcoma corporis uteri the tumour was egg-sized and originated in the posterior wall. It penetrated the wall at several places with tumour thrombi in the blood vessels of the portio and in the parametrium.

No metastases in the tubes were found in any of these cases. The tubes measured from 4–8 cm. in length. Their diameter varied from 0·5–1 cm. In 18 of the cases of adenocarcinoma cutting open the lumen of the tubes revealed nothing pathological macroscopically. In 7 cases there was stenosis of the lumen of one of the tubes 0·5–2 cm. from the uterine end.

It should be pointed out that in one case of adenocarcinoma of the body one of the tubes had been extirpated previously, yielding a total of 49 tubes for examination from this condition. In the one case of sarcoma the mucosa of the tubes revealed no pathological macroscopic alterations.

Several sections were made from all of the tubes for histological examination, and some of them were mounted in their entirety.

In one case the right tube was the site of the primary tumour. The tumour was situated in the distal part of the tube, 2 cm. from the uterus and measured 8×4×2 cm. It was greyish white and

of a soft consistency. The other tube appeared normal.

The ovaries were generally of almond size except for one case where a benign teratoid cyst the size of a grapefruit was found in one of the ovaries. In no case were tumour metastases demonstrated in the ovaries. There were some fibrous and/or ordinary follicle cysts.

The tubes and ovaries were received separately for examination, as they were pinched off with forceps and extirpated with the least possible manipulation of the uterus. The tubes were examined immediately after removal. The pinched-off, uterine portion was cut away, about 0·5 cm. in length, and the tubes were then irrigated with 20 ml. physiological saline. A record syringe with a thick needle was employed. After irrigation the tubes were cut open and 3 or 4 direct smears were made from the mucous membrane by rubbing a slide on the surface. The water flushed through the tubes was centrifuged and several smears were made from the sediment, sometimes as many as 8. All of the smears were fixed in equal parts of alcohol/ether and stained ad modum Papanicolaou.

In the 7 cases where there was a stenosis in one of the tubes, an incision was made just lateral to the stenosis in 5 cases and the lateral part of the tube was flushed; in the 2 other cases only direct smears were made. In one case only direct smears were made from the mucous lining of the tubes. Thus there is a total of 4 tubes from which only direct smears have been made and none from the washings.

In 20 of the examined cases of adenocarcinoma corporis uteri we also had washings from the Douglas fossa as this had been flushed with saline immediately after opening the abdomen and the washings were aspirated and collected. After being centrifuged the sediment provided material for smears. The number of smears for one case varied from 3 to 7 according to the amount of sediment.

Results

The normal cell flora in cytological preparations from the mucous lining of the tubes shows single cells, usually cylindrical, or they may lie in groups and are then mostly round to oval in shape. The cells have basophile or weakly acidophile cytoplasm. The nuclei are round or oval, rather uniform in size and with an even, fine network of chromatin and regular nucleoli. In only a few cases were tubular epithelium cells with intact cilia observed (Figs. 1 and 2). This is what one would expect in material from these age groups. The mucous lining of the tubes as well as of the uterus is under hormonal control. The epithelium has two main cell types—with and without cilia—the latter are secreting cells. The cell flora becomes more uniform after the menopause as the cilia disappear and secretion ceases.

In some of the smears in the material examined there were also some highly atypical cells which are interpreted as tumour cells. These varied in size, but all are enlarged. They are round to oval or polygonal in form. The cytoplasm is basophile and, in some cases, vacuolized. The nuclei are mostly very large, irregular in shape and some are hyperchromatic. There is often a coarse chromatin network and large, irregular nucleoli. No mitotic tumour cells were observed. Some of the cells are solitary and have well defined limits, some lie in groups (Fig. 3). In the latter case their limits may be confluent. There are also some cells which show signs of degeneration with vague, poorly defined delimitation, weakly staining cytoplasm and with pyknotic or swollen nuclei.

Among the 25 cases of adenocarcinoma corporis uteri, tumour cells were demonstrated in the tubes of 15. In 8 of these cases the tumour cells were found in both tubes. In 4 of these there were large tumours which filled the entire uterine cavity, while in the other 4 there were small or medium tumours. In the remaining 7 cases tumour cells were demonstrated in one tube only. Among these there was a more limited tumour in 4 cases, while in 3 the tumour tissue filled the entire uterine cavity.

In the smears from sarcoma corporis uteri cells were found in both tubes, and in the case with carcinoma of the tube there were tumour cells in the other tube.

Tumour cells were demonstrated both in washings from the tubes and in direct smears

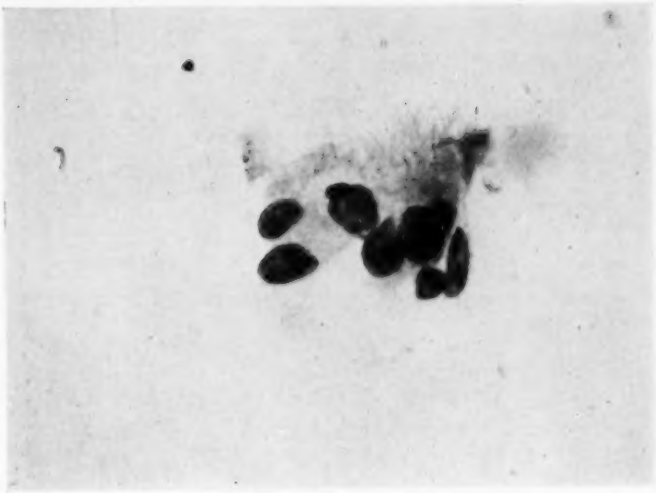

FIG. 1
Ciliated epithelial cells from Fallopian tube. Patient aged 49 years.

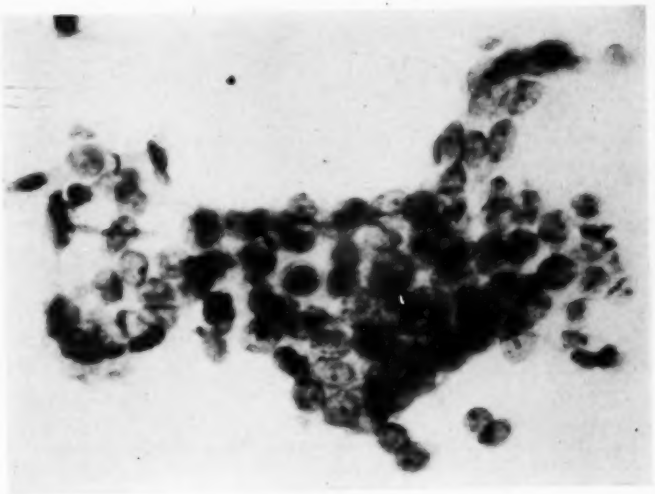

FIG. 2
Unciliated cells from Fallopian tube.

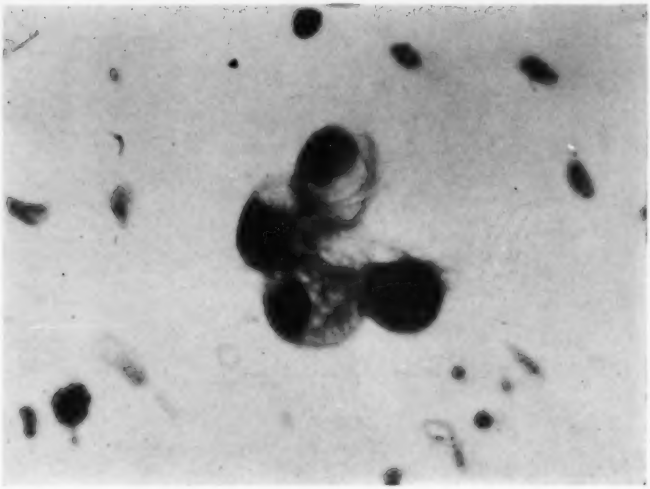

FIG. 3
Adenocarcinoma cells in washings from tube.

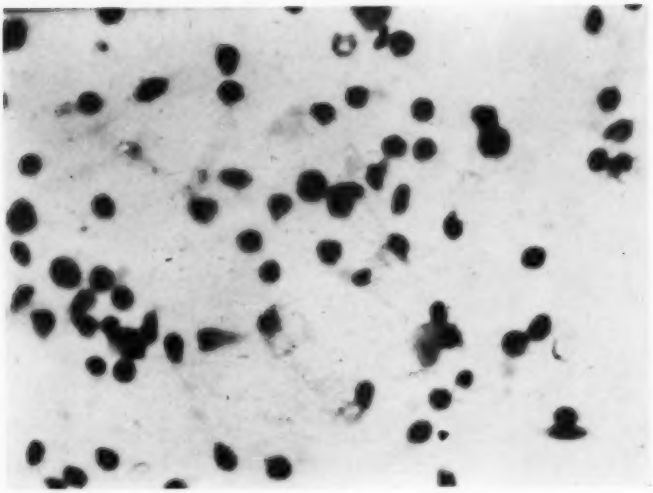

FIG. 4
Normal cells in washings from the pouch of Douglas.

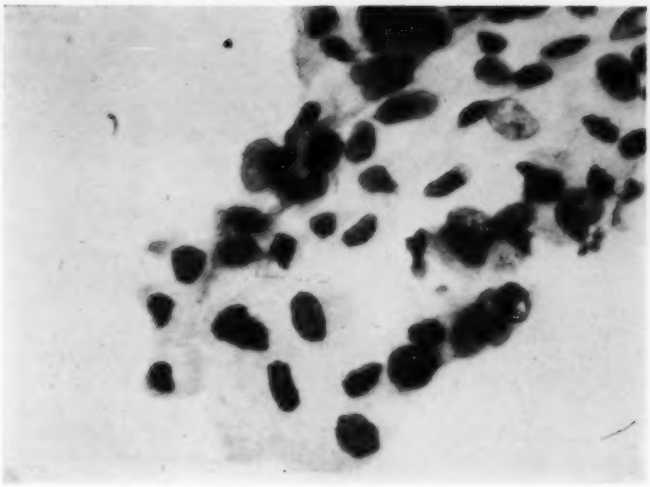

FIG. 5
Cancer cells in washings from the pouch of Douglas.

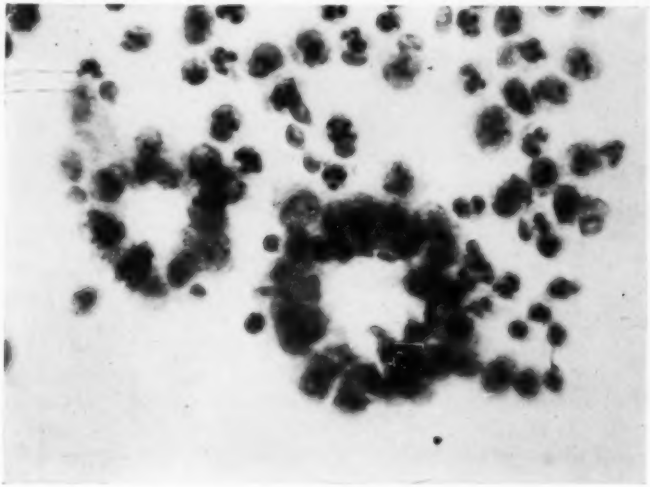

FIG. 6
Cancer cells with intact nuclear structure in washings from the pouch of Douglas.

from the mucous lining. It is of interest to compare the efficiency of these two methods. As mentioned above, the material includes a total of 49 tubes from adenocarcinoma corporis uteri. Four of these tubes were not flushed. There are thus 45 tubes available for comparison of the methods. The washings from 8 of these tubes revealed no tumour cells while direct smears showed 3 cases with tumour cells (positive) and 5 negative. For 30 tubes the two methods gave the same results, in 7 tubes the results differed. The washings from these 7 tubes gave 4 positive and 3 negative results, and the direct smears gave the converse results. In the case of sarcoma the same positive result was obtained by the two methods in both tubes.

In the case of primary carcinoma of the tube there was normal cell flora in the washings from the other tube while the direct smear revealed atypical cells.

It thus appears that the best results are obtained by employing both methods as either may be negative.

In the cytological preparations from the pouch of Douglas there are mesothelium cells, histiocytes, leukocytes and erythrocytes (Fig. 4). In some cases there are also atypical cells, either solitary or in groups. They have the same appearance as the atypical cells in smears from the tubes and are undoubtedly tumour cells. Some cell groups exhibit definite glandular structure (Figs. 5 and 6).

As mentioned above, washings from the pouch of Douglas were examined in 20 cases of adenocarcinoma corporis uteri. Tumour cells were found in 6 of them (positive), 9 cases showed normal cell flora (negative) and in 5 cases there were no cells at all in the preparations.

Among the 6 positive cases tumour cells were also found in smears from one or both of the tubes in 5. In the 6th case with positive result in the washings from the Douglas pouch there was normal cell flora in the smears from the tubes. This suggests the possibility of spreading to the peritoneum by other routes than the tubes. There was a large tumour in the uterine cavity which infiltrated the muscular layer to a depth of 3 mm. from the serosa side, although no serosa infiltration could be demonstrated microscopically. Direct spreading from the tumour to the peritoneal cavity from a perforated uterine wall is thus improbable.

In addition to these cases it can be mentioned that similar examinations were made in two cases with the histologic diagnoses: "Uterus with malignant portio tumour. Carcinoma probable", and "Uterus with slight irregular adenomatous hyperplasia of the mucous lining of the corpus". In these two cases no tumour cells were found either in the washings from the Douglas pouch or in washings or direct smears from the tubes.

Concluding Remarks

There is, to the author's knowledge, no previous cytological investigation as to the possible superficial spreading to the tubes or peritoneum from corpus cancer through the tubes.

The present investigation of 25 cases of adenocarcinoma corporis uteri revealed tumour cells in the tubes in 15 cases, 8 of them bilateral.

In 6 of 20 cases examined there were tumour cells in the washings from the pouch of Douglas.

In one case of sarcoma corporis uteri there were tumour cells in both tubes, while the washings from Douglas fossa were not examined. In one case of carcinoma in one of the tubes with metastases to the uterine mucosa, tumour cells were demonstrated in the other tube, while washings from the fossa of Douglas were not examined in this case.

There seems to be no doubt that cells from cancer corporis uteri in a very large percentage of cases may spread superficially to the tubes and through them also to the peritoneum. A sharp distinction should be made between possible implantation of tumour cells and the development of tumour metastases. The latter requires that the implanted tumour cells have the necessary growth requirements. In this connexion it is significant that, in addition to tumour cells with regressive changes, there are also numerous tumour cells which appear fully viable judged by ordinary criteria. It is generally assumed that growth of implanted carcinoma

tissue will occur more readily where there are groups of cells, while solitary cells will perish. It is therefore significant that not only solitary carcinoma cells but also groups of cells are found in the smears.

The superficial dissemination therefore seems to afford possibilities for metastasis to the tubes and peritoneum.

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OBSTETRICAL MANAGEMENT IN ACHONDROPLASIA

BY

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TYPICAL achondroplasia is an uncommon condition. Infants affected by this anomaly show a high mortality during the first few months of life. In a large series of 60,000 deliveries at the Chicago Lying-in Hospital there was only 1 survivor out of 8 typical achondroplastic children (Potter, 1952). At the Hadassah University Hospital, out of 26,309 deliveries in the past 15 years, 4 achondroplastic children were born of whom 1 only survived. It is generally agreed that this pathological entity is caused by genetic factors and it has been shown that, when once occurring as a mutation, it is passed on as a rule as a Mendelian dominant to the offspring.

The rarity of the survival of typical achondroplastic children is the reason for the following report. The case is also of interest in that the parents were both achondroplastic dwarfs.

CASE REPORT

Two achondroplastic dwarfs, unrelated to each other, had been married for one year. Both were Jews of Syrian origin. The wife was born at term after a pregnancy which was complicated by toxaemia. Soon after delivery it was noticed that she had an unusually large head. The other 3 siblings in her family were all normal. During the first 2 years of life she was repeatedly ill, but no information about the nature of her disease could be obtained. At the age of 10 years the unsatisfactory development of the girl was first noted by her mother, and medical advice was sought. Menarche occurred at the age of 13 and subsequently she menstruated regularly every 4 weeks for 3–4 days.

At the age of 26 she married an achondroplastic dwarf also 26 years of age who showed considerable difficulty in locomotion due to gross deformity of the legs (Figs. 1, 2). He also had bilateral inguinal hernia but was otherwise well. Neither of his parents nor any other member of his family were affected by a similar anomaly. His parents were first cousins but were entirely normal. He himself had 11 siblings all of whom died, some immediately after delivery, others between the ages of 2 and 8 years. The cause of death in these children is unknown but most of them apparently were abnormal; the exact nature of the defect could not be elicited.

A few months after their marriage the wife became pregnant for the first time. She was delivered by Caesarean section at another hospital early in the seventh month of pregnancy after supposed onset of labour. The male child weighed 1,160 g., was 36 cm. in length and appeared to be achondroplastic. Though born alive, it expired after 35 minutes. No post-mortem was performed.

She became pregnant again 3 months later and was seen at our prenatal clinic in her third month. The pregnancy was uneventful till the sixth month, when she had to be admitted to the ward because of low back and pelvic pain which simulated onset of labour (Figs. 3, 4). She remained in the department under very strict supervision. During this time she suffered frequent attacks of discomfort and lower abdominal pains which on careful observation did not prove to be real labour pains. In the 36th week of pregnancy, she went into true labour characterized by severe contractions. Caesarean section was immediately performed and at the time of laparotomy the uterus showed signs of imminent rupture. A male infant was delivered which cried immediately; his length was 39 cm. and his weight 1,980 g. It was noticed that his head was disproportionately large, his extremities very short and there was syndactyly present between the 2nd and 3rd finger of the left hand (Fig. 5). X-ray pictures of the skeleton showed typical chondrodystrophic changes of mild degree (Fig. 6). The child was discharged from hospital after 6 weeks in good general condition, weighing 2,580 g.

COMMENTS

Chondrodystrophic dwarfism in humans is a hereditary abnormality considered to be a dominant mutation, the incidence of which has

been estimated at 1 in 12,000 births. This figure, arrived at by Mørch (1941) and accepted by Haldane (1949), has lately been questioned and the mutation rate of chondrodystrophy has been suggested as being in the neighbourhood of 1:100,000 (Slatis, 1955).

The low survival rate of chondrodystrophic children has been explained as due to abnormal bone proliferation in the region of the occipital foramen and subsequent compression of the spinal cord on the one hand and by pulmonary hypoplasia secondary to the chest deformity on the other. In the case of chondrodystrophic children born to mothers affected by the same disease, another most decisive factor, prematurity, may contribute to the high infant mortality. The severe antero-posterior contraction of the chondrodystrophic pelvis not only constitutes an absolute obstacle for vaginal delivery but also is the cause of false labour pains owing to the lack of sufficient space for the growing uterus. Therefore the infants are delivered as a rule by premature Caesarean section undertaken because of false pains. Because of the special anatomical conditions the distinction between false pain and real labour contractions is often most difficult, but of vital importance, as in the latter case uterine rupture may occur. For this reason we consider it to be absolutely necessary that the pregnant patient affected by chondrodystrophia be hospitalized from the sixth month at least or sooner where facilities for immediate Caesarean section exist. Only under such conditions can Caesarean section safely be delayed as long as possible to give the infant the maximal chance of survival. To ensure the viability of the child in these patients is of great importance as the emotional attachment of the parents to an achondroplastic child does not differ from ordinary parent-child relationship. In addition it has to be kept in mind that the majority of children born to chondrodystrophic parents are normal. According to Mørch (1941) 108 chondrodystrophic dwarfs altogether produced 27 children of whom 17 were normal and only 10 chondrodystrophic.

Franchini and Zanis (1910) report two chondrodystrophic parents, whose only child was also chondrodystrophic. The reason for the low incidence of chondrodystrophic children born to two affected parents may be that the homozygous foetus is probably of low viability and may be aborted early in pregnancy. Therefore the number of dwarfs resulting from new mutations was found to be four times that of hereditary chondrodystrophic infants born to parents suffering from the same disease (Mørch, 1941).

It is of interest to compare the rate of appearance of new chondrodystrophics in the communities of Israel with the rate observed by Mørch (1941) in a lying-in hospital in Denmark. Mørch found 8 new chondrodystrophics among 94,075 births in Copenhagen, whereas the Hadassah University Hospital, Jerusalem, during 15 years recorded 3 chondrodystrophic babies from normal parents among 26,309 births. The excellent agreement between these two rates ($X^2=0{\cdot}15$, $p=0{\cdot}7-0{\cdot}5$ without Yates's correction, $X^2=0{\cdot}0053$, $p=0{\cdot}95-0{\cdot}90$ with Yates's correction) deserves attention, in spite of the well-founded objections raised by Slatis (1955) against calculations of mutation frequencies based on such data.

Summary

An achondroplastic dwarf, born to parents affected by the same disease and which survived, is presented.

The obstetric management of chondrodystrophic mothers is discussed.

We are indebted to Prof. B. Zondek, for helpful suggestions, to Dr. E. Goldschmidt of the Hebrew University Department of Zoology for help in the statistical evaluation and to Dr. S. Shorr for the interpretation of the X-ray films.

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FIG. 1

Male chondrodystrophic dwarf. Height 106 cm. Note large right inguinal hernia. (The father.)

FIG. 2

The chondrodystrophic pelvis, spine and hip joints of father. Note the severe changes in the heads of both femora. Sagittal position of the sacral bone.

FIG. 3

Typical female chondrodystrophic dwarf in six month of pregnancy. Height 111 cm. (The mother.)

FIG. 4

The chondrodystrophic pelvis, spine and hip joints of mother. Note the small deformed pelvis. Sagittal position of the sacral bone.

FIG. 5
Chondrodystrophic male infant.

FIG. 6
Slight chondrodystrophic changes of the proximal parts of both humeri and femora.

SPONTANEOUS EXPULSION OF GANGRENOUS UTERUS AFTER LOWER SEGMENT CAESAREAN SECTION FOR OBSTRUCTED LABOUR

BY

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GANGRENE of the uterus associated with pregnancy or parturition is commonly due to gas gangrene infection by *Clostridium welchii* and less commonly by other anaerobic organisms. In the early months of pregnancy it usually follows attempts at criminal abortion or an infection of a retained portion of placental tissue. At term gas gangrene of the uterus may follow death of the foetus with or without surgical interference; other cases are caused by prolonged difficult labour involving much trauma and sepsis. Rendle-Short (1942) reviewed 180 cases of gangrene of the uterus due to *Cl. welchii* infection.

In the case that is now reported gas gangrene was absent and no gas-producing organisms were isolated. The entire uterus was gangrenous and followed a lower segment Caesarean section performed on a septic uterus containing a macerated foetus. After a careful search of the literature the only comparable case we can find is that reported by Welply and Chen (1950), in which a Chinese primigravida, aged 20, who had been in labour for 36 hours, had a lower segment Caesarean section performed for obstructed labour. A live hydrocephalic infant weighing 10 pounds 11 ounces (4,848 g.) was delivered. The patient had a very stormy convalescence and a profuse pure growth of *Bacterium coli* was isolated from a cervical swab. Penicillin and sulphonamides were given from the start without much effect. The patient complained of increasing abdominal pain with an offensive purulent vaginal discharge. On the 18th day of the puerperium the temperature rose to 103° F., and a large tender mass was found in the left iliac fossa. The following day a piece of fleshy tissue protruded for 2 inches out of the vagina. It was dusky-red, sausage-shaped and covered in pus and it was attached to a broad flat piece of tissue passing through the cervix. Twenty days after the original operation the abdomen was re-opened and a large abscess cavity was found from which a pint of foul watery pus had previously been expressed on vaginal examination. The whole ring of the cervix could be seen from above. The prolapsed mass was drawn up and found to be a sequestrum of the supracervical non-involuted dead uterus. The histological report showed dead uterine muscle but no gas gangrene. Healing was complete a month later.

CASE RECORD

N.S., an African primigravida, aged 19, was admitted as an emergency to the Provincial Hospital on 28th December, 1954. She was at term; she had not received any antenatal care but she had been well during her pregnancy. Labour had begun 4 days earlier at home and foetal movements had been absent for 3 days.

On admission to hospital the patient's condition was poor and she looked toxic and exhausted. She was small, slightly built and ill-nourished. Her temperature was 101° F., pulse rate 160 per minute, blood pressure 104/65 mm. Hg and albumen was present in the urine. The uterus, which was in a state of inertia, contained a full-time foetus in the right occipito-posterior position. The head was engaged; the foetal parts were easily palpable and the lower uterine segment extended well above the symphysis pubis. No foetal heart sounds were heard. On vaginal examination the cervix was found to be fully dilated; the membranes were ruptured; a large caput was present over the vertex and there was definite contraction of the outlet.

Treatment. Penicillin 1,000,000 units and Streptomycin 1 g. were given at once and a blood transfusion com-

menced. The patient was then examined by the Registrar, Dr. J. Green, who decided that in view of the patient's unsatisfactory condition a lower segment Caesarean section would be a safer procedure and cause less shock than a difficult craniotomy.

Two hours after the patient's admission to hospital the operation was begun under nitrous oxide, ether and trilene anaesthesia. The lower segment was thin and stretched out. A Bandl's ring was present about 3 inches (7·5 cm.) above the symphysis pubis. The lower segment was incised transversely and a macerated female foetus weighing 7 pounds 5 ounces (3,317 g.) was delivered without any difficulty. The uterine contents were foul-smelling and purulent. After their removal the uterine incision was sutured in the routine manner in 3 layers and a rubber-tube drain inserted into the pelvis for 48 hours. In view of the highly septic condition of the uterus a hysterectomy had been considered by the surgeon, but, as the patient was a young primigravida, he decided on trying to conserve the uterus with the aid of antibiotics.

Post-operative treatment. At the end of the operation the patient was very shocked and the blood pressure was imperceptible. An intravenous drip of 8 ml. of 0·1 per cent Levophed in 1,000 ml. of 5 per cent dextrose was set up. Concurrently a blood transfusion of 1,100 ml. was in progress. The next day, 29th December, 24,000 units of anti-gas-gangrene serum were given intramuscularly and gastric suction (Wangensteen) was started.

For the first 2 days after the operation the intravenous drip was maintained as above, as the patient's condition remained very critical and at times the blood pressure could not be recorded. Once a day an ampoule each of Lyobecin and Terramycin (250 mg.) were added to the vacoliter. Penicillin 500,000 units and Streptomycin 0·5 g. were given twice daily for the first 12 days. From the third to the fifth day (31st December, 1954 to 2nd January, 1955) the amount of Levophed in the vacoliter was halved while the rate of flow was gradually reduced. The drip was discontinued after 5 days.

The remainder of the post-partum period continued to be stormy; the abdominal wound discharged pus and the lochia was very offensive. In spite of the antibiotics the uterine sepsis did not subside and the temperature on the 13th day (10th January) rose to 103·6° F. A culture of the vaginal swab showed the presence of *Bacillus proteus*, which was slightly sensitive to Chloromycetin and from the abdominal wound haemolytic staphylococcus albus, sensitive to Erythromycin and Chloromycetin, was isolated.

The patient was transferred to the newly opened Livingstone Hospital on 12th January, 1955. The uterus was easily palpable as a hard mass at the level of the umbilicus and a purulent discharge was draining freely from the vagina. In view of the sensitivity tests, Chloromycetin (250 mg.) was given 6-hourly. The temperature began to settle but the uterine condition remained unchanged and pus continued to pour out. On 20th January it was decided that, as no further progress was being made with the antibiotics, Hobbs's glycerine irrigation treatment should be given a trial. A rubber catheter was passed into the uterus and sutured to the cervix. One ounce (28 ml.) of 0·1 per cent Acriflavine in glycerine was instilled every 6 hours. The patient's general condition began to improve slowly and the temperature did not rise above 99° F. but on the 28th January it rose to 100° F. On the 30th January, 33 days after the Caesarean section, she passed a large necrotic mass, the size, shape and appearance of a subinvoluted uterus (Fig. 1).

On bimanual examination the abdominal mass had completely disappeared. There was no cervix palpable but the suture holding the catheter was still in position and it was removed together with the catheter. After this event the temperature settled once more. The abdominal wound had healed and the vaginal discharge had ceased by the 26th February, on which day the patient was discharged from hospital. She was asked to return 2 weeks later for a further examination.

On the 15th March, 1955, under general anaesthesia a vaginal examination showed that the cervix had disappeared except for some lacerated scarred mucosa round the external os, which was practically level with the vault of the vagina. The body of the uterus could not be felt and there was some thickening of the fornices. The uterine sound passed for its full length through the external os without meeting any resistance. The dilators were then passed up to No. 12, which was easily moved about in every direction. The patient was discharged 2 days later and returned on 31st March for an X-ray examination of the pelvis.

A cannula was passed through the external os and 15 ml. of Viskiosol were injected (Fig. 2). The report stated: "There is no evidence of any normal shaped uterus. The dye appears to be in a potential space, but is not typical of any known uterine shape." It would appear that the cavity left after the expulsion of the uterus had shrunk considerably in the 2 weeks that had elapsed between the examination under anaesthesia and the X-ray examination. When the patient was subsequently seen in the Out-patient Department, she had completely regained her health and she showed no symptoms of ovarian deficiency.

Specimen. On gross examination the uterus measured 14 cm. in length and 7 cm. in breadth and the myometrium varied from 2 to 3 cm. in thickness. The cavity of the uterus was rough and irregular and covered in parts by loose shaggy tissue; no healthy mucous membrane could be seen. The inner half of the myometrium was pale, soft and necrotic. The external surface of the uterus lacked the normal smooth appearance and was somewhat irregular; the serous coat was absent. The line of separation had apparently been subperitoneal. The sites of attachment of the round ligaments were ill-defined and those of the Fallopian tubes could not be identified. The Caesarean section incision across the lower segment had healed.

Histological report. No endometrium was present and the myometrium was necrotic.

Comment

The two main factors responsible for moist gangrene are loss of blood supply and bacterial

FIG. 1
Section of gangrenous uterus.

FIG. 2
Cavity in pelvis 2 months after expulsion of uterus. Note absence of cervix.

infection. Although gangrene of an organ usually follows interference with the blood circulation, Welply and Chen (1950) thought it unlikely to occur in a puerperal uterus with its four main vessels and free anastomosis. In obstructed labour the capillary system probably undergoes repeated forced emptying with each violent contraction and this sets up a severe ischaemia with damage to both capillaries and muscles. In their case they suggested that this might have happened together with a low grade *Bact. coli* infection and aggravated by stasis due to operative trauma and to prolonged pressure by a large head.

Although this may explain the pathological picture in their case with the gangrenous process confined to the body of the uterus, it does not offer a satisfactory explanation in ours. Examination of the specimen showed that the transverse incision across the lower uterine segment had united, from which one infers that an adequate blood supply was maintained for at least a week after the operation. It is suggested that the chief factor was the severe infection which was confined to the decidua for some time and was partially controlled by the antibiotics. It then spread as a low grade mixed infection to the myometrium with involvement first of the terminal vessels and finally of the main vessels, until the gangrenous process was complete and ended with subperitoneal separation of the uterus and its extrusion. Additional factors were the patient's lowered vitality and the prolonged labour, but there was no evidence of traumatic interference with the blood supply.

It is reasonable to assume that the survival of Welply and Chen's patient and of ours was largely due to the antibiotics. Without them it is unlikely that either patient would have survived the stormy post-operative period and death from some form of sepsis or toxaemia would have been the probable outcome. Although neglected and grossly infected cases of obstructed labour are still to be found among the more primitive races, some of whom eventually reach hospital, it is not surprising that no case of gangrene of the uterus following Caesarean section was ever recorded in the days before antibiotics. Some of these neglected cases were treated either by Caesarean hysterectomy or craniotomy, and of those treated by Caesarean section some managed to survive but the remainder died from septicaemia, peritonitis or other complications. One is tempted to believe that the sequence of events in the 2 cases under discussion was only made possible because the more virulent organisms were killed by the antibiotics and the remaining pathogenic organisms, insensitive to antibiotics, were able to flourish and continue the low-grade infective process.

Summary

(1) Gangrene of the uterus after lower segment Caesarean section for infected obstructed labour is described in a young African primigravida.

(2) The whole uterus was passed spontaneously *per vaginam* 33 days after the operation following a stormy puerperium.

(3) It is suggested that the main factor in producing the gangrene was a low grade mixed infection by organisms insensitive to antibiotics. No gas gangrene organisms were isolated.

(4) The only other comparable case is the one described by Welply and Chen, in which the gangrenous body of the uterus was extruded as a sequestrum from the vagina and was subsequently removed at laparotomy.

I wish to thank the resident medical staff and the nursing staff of the Provincial Hospital and of the Livingstone Hospital for the care and attention given to this patient and for their co-operation.

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OBSTETRICAL-GYNAECOLOGICAL EPONYMS: ALEXANDER SKENE AND THE PARA-URETHRAL DUCTS

BY

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MORE than two centuries elapsed between the first description of the para-urethral ducts in women and their re-discovery by Alexander Skene, for whom these structures are now named. As early as 1672 Reinier de Graaf, in his *De mulierum organis* . . ., had recorded his observations on the paired "lacunae situated at the termination of the urinary passage", which, by analogy with the male, he assumed to be the excretory ducts of the female prostate. According to de Graaf, these ducts were the source of the lubricating fluid discharged from the woman's parts when she is sexually stimulated, and also the focus of gonorrhoeal infection. In one of his dissections of a woman who had had gonorrhoea, he described the diseased condition of "the glandular body embracing the urethra", while the uterus and vagina appeared normal. Purulent discharge from the para-urethral ducts was regarded by de Graaf as pathognomonic of gonorrhoea, which he sharply distinguished from other causes of leucorrhoea by this criterion.

De Graaf's notion that the coital fluid secreted by women was discharged through the urethra by way of the para-urethral ducts was corrected by Caspar Bartholinus in 1677, when he described the glands that now bear his name and explained their function. The para-urethral ducts rapidly faded into temporary oblivion and were not heard of during the next 200 years.

Skene was obviously unaware of the observations of the 17th century anatomists, for, when he announced his own discovery of the para-urethral ducts in 1880, he stated that he had been unable to find any reference to them in any of the textbooks of the day. "So far as I know," he wrote, "the anatomy of these glands has not been described, nor have the diseases to which they are subject been referred to by pathologists." Later in his paper Skene stated, "I know nothing about the physiology of these glands. They serve some purpose in the economy, no doubt, but what is their function is a question to be answered in the future."

The circumstances that led to Skene's discovery are related in graphic detail in this case report: "The patient was a married lady, 30 years of age. She was well developed, and had always enjoyed good general health. With the exception of a mild form of dysmenorrhea, she had had no disease of her sexual organs until one year before she came under my observation. At that time she was abruptly attacked with a profuse leucorrhea, and other symptoms of inflammation of the vulva and vagina, including painful urination. She placed herself at once under the care of her family physician, who treated her locally until she came to me. Her leucorrhea had, by that time, diminished and the painful urination had passed away, but otherwise she had not improved. At my first examination I found traces of the former inflammation of the vulva and vagina. The meatus urinarius was everted and surrounded by a number of papillary projections, of a deep-red color, and altogether presenting an appearance resembling that which is known as vascular tumor, or caruncle of the meatus. . . .

"The diagnosis then made was subacute vaginitis, perhaps of gonorrheal origin, and inflamed papilloma of the meatus urinarius. The vaginitis was treated in the usual way, and soon it terminated in complete recovery, but the inflammation and tenderness of the meatus remained unchanged, and annoyed the patient

FIG. 1
Alexander Johnston Chalmers Skene (1838–1900).

THE ANATOMY AND PATHOLOGY OF TWO IMPORTANT GLANDS OF THE FEMALE URETHRA.

BY

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(With lithographic plate.)

UPON each side near the floor of the female urethra, there are two tubules large enough to admit a No. 1 probe, of the French scale. They extend from the meatus urinarius upwards, from three-eighths to three-quarters of an inch. Figure 1 is a drawing from a section of the urethra, laid open by division of its posterior or vaginal wall. The tubules, having been distended by probes passed into them, are plainly seen

Figure 2 shows the same thing from the opposite side, the urethra having been laid open by section of its anterior wall. The space between the tubules is the floor of the urethra. From these it will be observed that the tubules run parallel with the long axis of the urethra.

They are located beneath the mucous membrane, in the muscular walls of the urethra. This is represented by Figure 3, which is a drawing taken from a transverse section of the urethra, about a quarter of an inch from the meatus.

The mouths of these tubules are found upon the free surface of the mucous membrane of the urethra, within the labia of the meatus urinarius. The location of the openings is subject to slight variation, according to the condition and form of the meatus. In some subjects, especially the young and very aged, and in those in whom the meatus is small and does not project above the plane of the vestibule, the orifices are found about an eighth of an inch within the outer border of the meatus. When the mucous membrane of the urethra is thickened and relaxed, so as to become slightly prolapsed, or

FIG. 2

Title page of Skene's paper announcing his discovery of the para-urethral "glands".

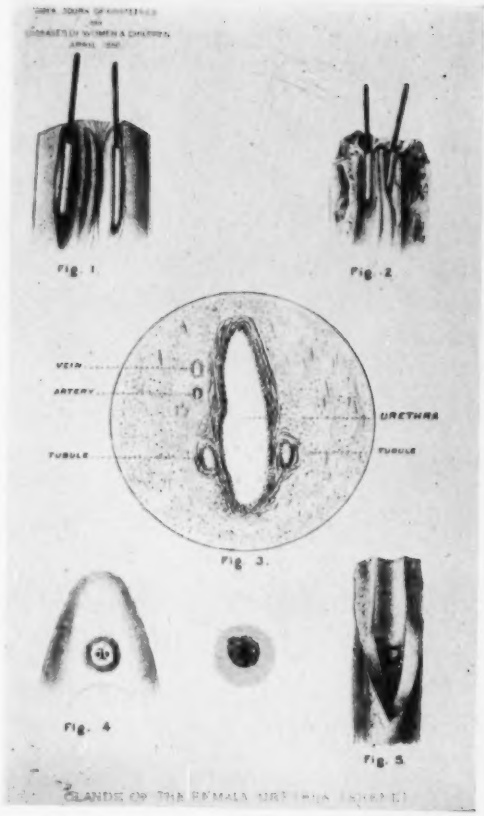

FIG. 3

Plate of illustrations from Skene's paper, showing the para-urethral ducts.

exceedingly. She could not walk or sit without pain, and coitus had to be avoided entirely.

"I presumed at first that the disease of the meatus was kept up by the irritating discharge from the vagina, and I hoped that when the one was removed, the other would get well, but such was not the case. I then thoroughly cauterized the elevated and tender points about the meatus with nitrate of silver. This caused very great pain at the time, and was followed by no improvement. Pure nitric acid was used in the same way, but with no better result, except to destroy elevations of the mucous membrane around the orifice. The same areola of inflammation around the meatus continued, and the symptoms remained the same. . . Suffice it to say that for eight months I treated the disease with diligence and care, but at the end of that time she was very little better.

"Caustics and cauteries being unsatisfactory, I tried sedatives and alteratives, including iodoform, iodine, mercury, and bismuth. At times the inflammation subsided slightly, and the elevated points became smaller, but in a short time fresh proliferations sprang up again, and the mucopurulent secretion continued to bathe the parts. Towards the end of this long period of treatment, and while making a critical examination, I observed that on each side of the meatus there were two depressions filled with a yellowish-gray matter, looking like minute ulcers, but upon probing them with a view to determine their depth, I found that they admitted the probe over half an inch. After withdrawing the probe, I made pressure upon the urethra from above downwards, and succeeded in expressing a purulent fluid which could be distinctly seen escaping from their orifices. Treatment was then directed to these canals; first they were injected with tincture of iodine, and subsequently they were cauterized by passing a probe, coated with nitrate of silver, along their entire depths. Prompt improvement followed this application. The inflammation around the meatus gradually subsided, and the pain and tenderness passed away. In less than two months from the time that a correct diagnosis was made, and appropriate treatment employed, the patient recovered completely. . . ."

Stimulated by his experience with this patient and another in whom prompter response to treatment was obtained, Skene undertook a systematic investigation of the para-urethral ducts in the patients thereafter coming under his care. His studies were almost entirely clinical, however, supplemented by only an occasional histological preparation; and he referred to the structures, promptly to be identified with his name, as glands rather than ducts. "I have called them glands," he stated, "because they differ in size and structure from the simple follicles found in abundance in the mucous membrane."

"When I first discovered these glands I presumed that they were mucous follicles that were accidentally of unusual size in the subject examined, but having investigated more than one hundred of these, in as many different subjects, and finding them constantly present, and so uniform in size and location, I became satisfied that they were worthy of a separate place in descriptive anatomy."

Skene's anatomical description is given in the first page of his paper (Fig. 2). Continuing with a consideration of the various pathological conditions to which the para-urethral ducts are subject, he wrote: "When the mucous membrane of the urethra is thickened and relaxed, so as to become slightly prolapsed, or when the meatus is everted, conditions not uncommon among those who have borne children, the openings are exposed to view upon each side of the entrance to the urethra."

Gonorrhoeal inflammation was correctly regarded by Skene as the most important pathological condition observed in these structures: "These glands may, I presume, become involved in any inflammation of the vulva, urethra or vagina, but from the history of the cases that have come under my observation I have been led to believe that the disease observed was caused by gonorrhea, and it persists in the glands long after all traces of the original disease has disappeared. Indeed, when this disease is once established, it has no natural tendency to recover."

Alexander Johnston Chalmers Skene was born in Aberdeenshire, Scotland, 17th June, 1838; but like James Douglas, William Smellie, and our contemporary Benjamin Watson, he forsook the green hills of his native land to seek

his fortunes elsewhere. After his early education in Aberdeen and King's College, Skene migrated to America at age 19. In 1860 he embarked upon the study of medicine, first at Toronto, and continuing in the University of Michigan and the Long Island College Hospital, from which he received his medical doctorate in 1863 and whose most famous alumnus he subsequently became. Skene spent the following year as Assistant Surgeon in the U.S. Army and is credited with formulating a plan for establishment of an army ambulance corps. He returned to Brooklyn and entered private practice in 1864, serving also as assistant to Austin Flint, Sr., while the latter was Professor of Practice at Long Island College Hospital. It is not clear at precisely what stage in his career Skene began to devote himself exclusively to gynaecology, but he presumably elected this specialization sometime before 1870, for it was in this year that he was appointed Professor of Gynecology in the Long Island College Hospital, where he served as dean from 1886 to 1893 and as president for the following 6 years. In 1883 he was also made Professor of Gynecology at the New York Post-Graduate Medical School. Skene's practice was prodigious. In 1884, in partnership with William M. Thallon, he opened a private sanatorium on President Street near Prospect Park in Brooklyn, and 5 years later he incorporated Skene's Hospital for Self-Supporting Women. Skene was a founding member of the American Gynecological Society and served as its president in 1886–87. A prolific writer, he explained the large volume of his literary output by his custom of writing at home in the early hours before breakfast, to avoid interruption. In addition to his many scientific articles, Skene was the author of 5 textbooks, of which his *Treatise on Diseases of Women* went into three editions and his *Diseases of the Bladder and Urethra in Women*, into two. He also invented or modified a number of surgical instruments, but his principal claim to fame lies in his re-discovery of the para-urethral ducts. Skene died in his summer home in the Catskills, 4th July, 1900, at age 62. Brooklyn's traditional partisanship and pride in its own extend to its adopted sons as well as the native born. After Skene's death Schroeder wrote of him: "This is a distinction that has never come to any physician located on Long Island: to have his name connected with any part of the human body." De Graaf's priority still lay unrecognized.

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CYSTADENOFIBROMA OF OVARY ASSOCIATED WITH ENDOMETRIOSIS

BY

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CYSTADENOFIBROMA is one of the rarer of ovarian neoplasms. The present case, a large tumour of 1,200 g., derives its interest from certain histological features and from its association with adenomyosis of the uterus and endometriosis of the transverse colon.

CASE HISTORY

An unmarried woman of 43 was admitted to hospital with a 24-hour history of intermittent epigastric pain radiating to the right iliac fossa. She had vomited twice. There were no other symptoms. Her menstrual periods had been irregular but not excessive or painful; 35 days had elapsed since the last one. Examination revealed tenderness in the right iliac fossa with hyperaesthesia and guarding. Temperature 98·5°, pulse 125.

A diagnosis of appendicitis led to laparotomy at which the appendix was removed. It appeared to be normal. There was, however, some free fluid in the peritoneum and exploration revealed a large mass in the transverse colon which was thought to be inflammatory. Biopsy of the mass was performed and the abdomen closed. The biopsy report was: "a rounded mass of soft tissue 2·5–3·5 cm. in diameter. There is a strand of muscle visible on the cut surface but the relation of the mass to the bowel cannot be made out with certainty. Sections show a highly cellular stroma with much inflammatory infiltration containing glandular spaces lined by columnar epithelium. The picture is reminiscent of endometrial glands and stroma." It might be added that the stroma shows a conspicuous decidual reaction (Fig. 4) and that glycogen can be demonstrated in the epithelial cells. Bacterial culture of the mass was sterile.

At a subsequent operation the mass was exteriorized and covered with muscle and skin extra-peritoneally.

She remained well until 3½ years later when on 3 separate occasions she had attacks of abdominal pain lasting a day or two and accompanied by nausea and vomiting. These attacks subsided but after another 6 months a more severe episode accompanied by abdominal distension was diagnosed as intestinal obstruction and laparotomy was performed. This revealed a large left ovarian cyst, which was adherent to the rectum, uterus and loops of bowel. During removal the cyst partly ruptured spilling dark, thin, blood-coloured fluid. At the same time the right ovary and a somewhat enlarged uterus were removed. Post-operative progress was satisfactory but a further acute episode suggestive of intestinal obstruction occurred some 3 months after operation.

PATHOLOGY

The ovarian tumour, as examined after fixation, was very approximately spherical with a diameter of about 130 mm. and a weight of 1,200 g. The pedicle was broad and no obvious remnant of ovarian tissue was to be seen. The external surface of the tumour was for the most part smooth, pale and shining, but was in places split up by clefts between which rather nodular or bulbous papillary processes emerged. The average diameter of these was about 10 mm. Around them were small patches of roughening and brown discoloration of the surface. Section revealed two main parts to the tumour; a lower predominantly solid portion, composed of translucent pale grey tissue with a coarse nodular pattern intersected by a few deep clefts, and an upper cystic portion which was deflated and much folded.

The wall of this cyst was 3–5 mm. thick and fibrous, with a rough brown inner lining composed of a thin layer of old blood clot. A few coarse bulbous processes projected into the proximal part of the cavity.

The Fallopian tubes and the right ovary (15×15×5 mm.) appeared to be normal.

The uterus, less the cervix, had a length of 90 mm. and was proportionately thick, the endometrium being 2 mm. deep and the myometrium of the fundus having a maximum thickness of 18 mm. A small tumour occupied the whole of the posterior wall of the fundus without, however, causing expansion of the

myometrium. Its closely whorled pattern was suggestive of a fibroid but the colour was pale yellow and the margin was indistinct. It appeared to measure about 15 mm. in each dimension. The remainder of the uterus was normal.

Microscopy of the uterus shows a normal proliferative endometrium. The tumour described is a patch of adenomyosis in which similar endometrium, with rather variable proportions of glands and stroma, extends to a depth of 15 mm. within the myometrium. The stroma both around the acini and where it appears to extend independently is, perhaps, rather more fibrous than is usual in adenomyosis. Collagen fibres are plentiful right up to the bases of the epithelial cells (see Fig. 3). No glycogen is demonstrable in any of the epithelial cells.

The ovarian tumour is composed for the most part of fibromatous tissue with alternating cellular parts merging into fairly densely collagenous areas with fibroblasts scattered only sparsely. The deep clefts in the tumour and the papillary projections are lined by a single layer of epithelium, and there is epithelium, too, forming groups of well-defined acini, within the substance of the tumour (Figs. 1 and 2). The cells vary in shape from cuboidal or even squamous to tall columnar cells sometimes with cilia and in places they contain subnuclear vacuoles which stain with P.A.S. and Best's carmine. Occasional mitotic figures are to be found in this epithelium but nowhere is there any nuclear hyperchromatism or other irregularity suggestive of neoplastic change. The greatest activity in the tumour seems to be in the fibroblastic stroma immediately beneath the epithelium. The plump and rather rounded cells in this region contain numerous mitoses.

With increasing distance from the epithelial surface the mitoses become fewer, the cells are more elongated and collagen is laid down until, in the parts remote from epithelium, collagen forms the bulk of the tissue. Haemorrhage into the cyst spaces and into the stroma complicates the picture in places.

Thus there are in this one case three areas of hyperplasia; typical adenomyosis of the uterus, endometriosis of the transverse colon in which a somewhat atypical stroma is probably due to decidual change complicated by acute inflammation and a tumour of the ovary called, descriptively, cystadenofibroma. The resemblance of the epithelium of the latter both morphologically and, in respect of glycogen, histochemically, to endometrium is striking.

Discussion

Cystadenofibroma is an uncommon ovarian tumour. Scott (1942) collected 13 cases at Baltimore from 26,000 gynaecological specimens in 20 years and smaller numbers have been recorded from time to time. The tumours range in size from hazel nuts to footballs and the larger ones at least seem to have a relatively late age-incidence, most of Scott's cases being within a decade of 60. In one case there was a chocolate cyst of the opposite ovary.

The association of cystadenofibroma of the ovary with endometriosis elsewhere has not, hitherto, been described. The close resemblance of the proliferative epithelial elements in the two conditions, their possible common origin, in the case of the ovary itself, from the germinal epithelium and the essentially benign nature of both types of hyperplasia might lead one to suppose that the association was not altogether fortuitous. The differences, however, are clear-cut. The absence of true endometrial stroma in the cystadenofibroma is one distinction, although frequently stroma is scanty in ovarian endometriosis. More significant is the fact that cystadenofibroma usually occurs after the menopause, implying thereby a lack of dependence on ovarian hormones. While this does not apply in the present instance, the features of the case are nevertheless most plausibly explained by coincidence.

On the other hand the rarity of cystadenofibroma and the relative uncommonness of multiple endometriosis combine to make this coincidence more noteworthy. If other similar cases come to be recorded the possibility of a common denominator would have to be considered. This might be in the nature of a common stimulus to hyperplasia, or it could be that the larger cystadenofibromata, which particularly seem to be found at a late age, have arisen as an

FIG. 1

Cystadenofibroma of Ovary. Groups of epithelial tubules within a very active fibroblastic stroma. ×200.

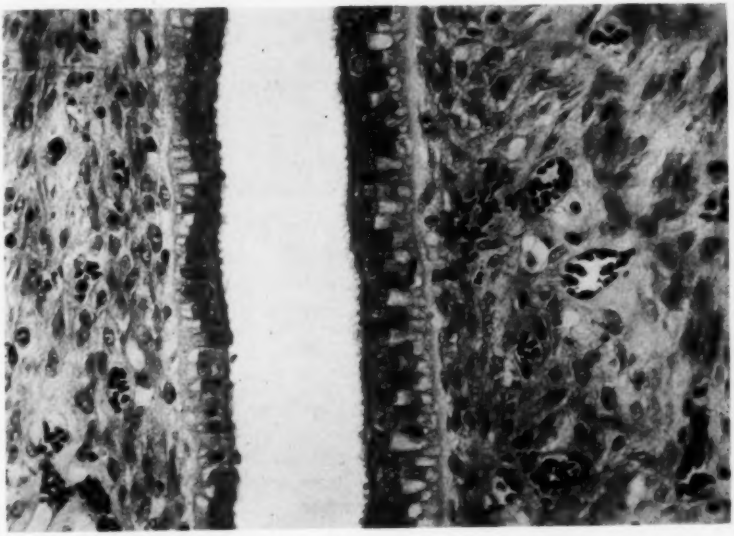

FIG. 2

Cystadenofibroma of Ovary. A cleft in the fibromatous part of the tumour lined by columnar epithelium mostly ciliated and with subnuclear vacuoles. ×400.

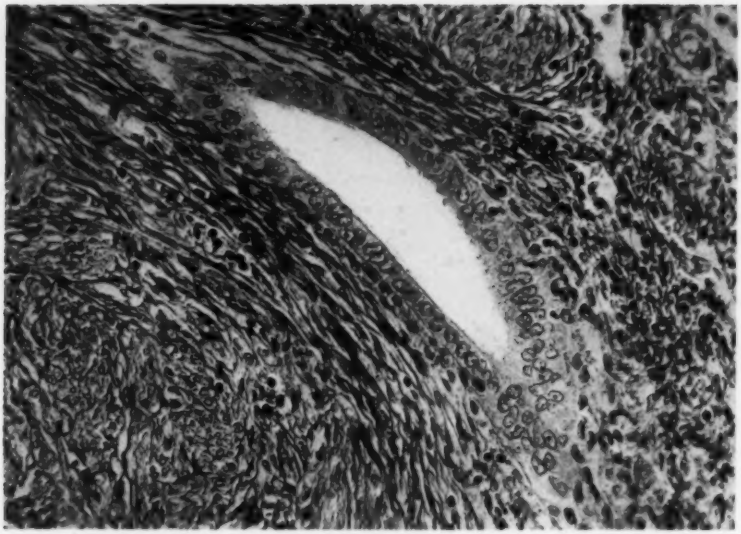

FIG. 3

Adenomyosis of the uterus (Van Gieson's stain). The stroma contains collagen fibres right up to the base of the epithelial cells. ×400.

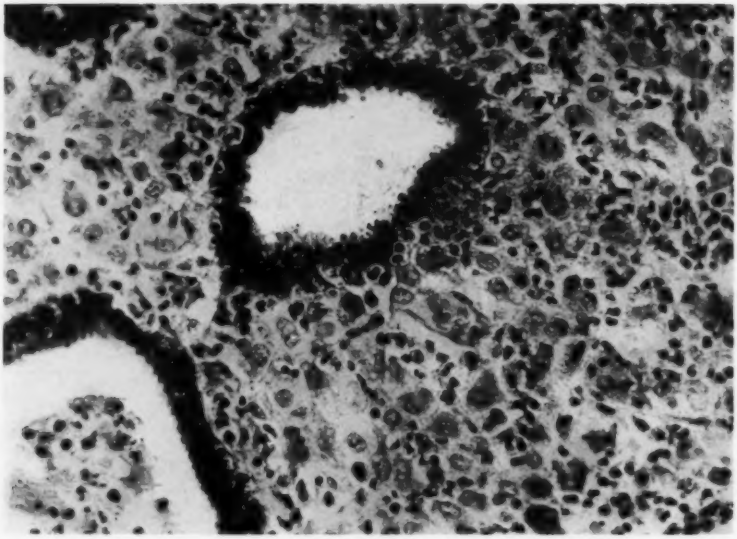

FIG. 4

Endometriosis in the wall of the transverse colon. There is a well-marked decidual reaction in the stroma. Diffuse and focal polymorph infiltration is present. ×400.

H.E.M.K.

autonomous development from pre-existing ovarian endometriosis.

ACKNOWLEDGMENTS

I am indebted to Mr. F. W. Harlow for permission to publish this case, to Dr. R. D. Clay for the report on the first specimen and to Mr. A. E. Clark for the photomicrographs.

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INTERSTITIAL CELL HYPERPLASIA OF THE OVARY ASSOCIATED WITH A BRENNER TUMOUR

BY

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THE presence of fairly compact groups of cells at the hilus of normal ovaries structurally identical to the interstitial or Leydig cells of the testis has been established mainly through the work of Berger (1923, 1945).

The occurrence of hyperplasia of these ovarian hilus or extra-testicular Leydig cells giving rise to masculinization has been recorded by three writers (Berger, 1945; Sternberg, 1949; Langley, 1954). We wish to report a fourth case of this condition associated with a Brenner tumour of the ovary and benign pathological hyperplasia of the endometrium with, however, only equivocal evidence of masculinization.

CASE HISTORY

Mrs. A.A., a widow, age 58, was first seen on the 15th November, 1955, complaining of vaginal bleeding of 5 days duration occurring two weeks previously. She had lost approximately one stone in weight over the past year. During the preceding 3 months there had been increasing facial hirsuties. Menstruation began at 14 and was quite normal until the age of 38 when she developed a severe menorrhagia which was treated with radium and followed by a 3-months course of oestrogens. No further vaginal bleeding occurred until November, 1955. There had been 2 pregnancies, one in 1923 and the other in 1925, both full-time normal deliveries. She had led a healthy active life and had never experienced any serious illnesses. On examination her general condition was good although there was evidence of some loss of weight. A moderate growth of hair was present on the chin and upper lip requiring shaving at least twice a week. The pubic and axillary hair distribution were feminine in type and the breasts were normal for a woman of her age. There were no voice changes. Her hair was falling out and had become rather coarse over the past 18 months. The vulva and vagina showed no appreciable senile changes. On pelvic examination the uterus and adnexae were found to be normal apart from a slightly bulky uterus. A general medical examination revealed no abnormal findings; her blood pressure was 155/90 mm. Hg.

A diagnostic dilatation and curettage was performed. This showed a benign pathological endometrial hyperplasia and a total hysterectomy and bilateral salpingo-oöphorectomy was carried out.

There was an uneventful convalescence and the patient was discharged home 2 weeks after the operation.

MACROSCOPICAL EXAMINATION

The uterus and cervix measured $9 \times 6 \times 5$ cm. A rounded intramural fibroid was present measuring 4 cm. in diameter. The endometrium was thickened and appeared cystic. There was a rounded, slightly bossed, firm yellowish-white tumour of the left ovary measuring $3 \cdot 5$ cm. in diameter. The right ovary was of normal shape but of size corresponding to that of a woman of child bearing age.

MICROSCOPICAL APPEARANCES

The endometrium showed the changes of benign cystic glandular hyperplasia (Fig. 1).

The tumour of the left ovary was a typical Brenner tumour (Fig. 2).

Right ovary. The ovarian stroma was well developed but presented no significant deviations from normal. There were present throughout the mesovarium and extending into the adjacent parts of the stroma, moderately compact groups of well defined eosinophilic cells (Fig. 3). These cellular foci varied in size from those containing only a dozen or so cells to much larger groups containing many hundreds. A very intimate

association with nerve fibres was sometimes seen (Fig. 4). Individual cells were rounded, oval or polygonal in shape and averaged 10 μ in diameter, although larger giant forms up to 50 μ in size were occasionally seen. The nuclei were vesicular, almost invariably single, and one or more nucleoli were present. The cytoplasm was finely granular and eosinophilic, occasionally containing brown pigment granules. Crystalloids of Reinke (Fig. 5) were seen in only two areas of the numerous sections examined. These are strongly eosinophilic bodies, rectangular in shape, measuring up to 50 μ in length. They sometimes show a pointed extremity and pairs may be found lying side by side (Fig. 6). They occurred in an intra- or extracellular location, the impression being that the latter position resulted from degeneration of the parent cell. Rounded eosinophilic intra-cytoplasmic bodies were also seen most commonly in the crystalloid areas and apparently related to them.

These cells and the crystalloids stained an intense red with Masson's trichome stain: some Sudan IV positive globules were present in the cytoplasm but no definite periodic-acid-Schiff positive material was present.

A diagnosis of hyperplasia of ovarian interstitial cells was made and this was confirmed by Dr. F. A. Langley at the Department of Pathology, St. Mary's Hospital, Manchester.

In view of the histological findings hormonal investigations were performed and the following results obtained:

Total neutral 17-ketosteroids, 4·0 mg. per 24 hours.

Oestrogens (bioassay), 140 international units per day.

Gonadotrophins, 10 mouse units per day.

Discussion

The occurrence of occasional groups of pink-staining cells at the hilus of normal ovaries has been recognized for many years. Originally considered as part of the chromaffin system (von Winiwarter, 1908; Kohn, 1928), they were later designated sympatheticotropic because of their intimate association with nerve fibres (Berger, 1942) and recognized by this author as identical morphologically with the interstitial cells of the testis. Sternberg (1949) has comprehensively reviewed the subject and he was able to find foci of interstitial cells in 80 per cent of normal ovaries, examining 4–6 sections of each ovary. In our experience these foci in normal ovaries are always small and limited to one or two groups in any particular section examined. We have been able to find only 4 cases in the literature of hyperplasia of these ovarian interstitial or hilus cells. In all 4 cases large numbers of these cells were present, scattered throughout the ovarian hilus of each ovary and extending into the mesovarium. The presence of numerous apparently separate cellular groups and the bilateral nature of the condition was indicative of hyperplasia rather than true neoplasia. Slight or moderate symmetrical enlargement of the ovaries has been found on all occasions. In our case the bilateral nature of the condition was not obviously evident as the Brenner tumour on the left side had resulted in a very considerable reduction of ovarian tissue. In spite of this, however, the interstitial cells were obviously increased in the small amount of ovary still present.

Typical intracytoplasmic inclusions are found in these cells identical to those present in normal testicular interstitial cells. They consist of yellow-brown lipochrome pigment granules, sudanophilic droplets, acidophilic spherules and crystalloids of Reinke. These latter bodies are found only in interstitial cells and immediately establish identity. They were originally described by Reinke in 1896 in testicular interstitial cells and their nature or possible function still remain unknown. They are rectangular or rod-like in shape occasionally showing pointed extremities and acidophilic in their staining. They are rarely present in large numbers and usually occur scattered haphazardly in rather localized areas; where one is found others will usually be seen in the near vicinity. Acidophilic intracytoplasmic spherules, as described by Sternberg (1949) and Langley (1954), were also present in our case and were most noticeable in the crystalloid areas. Transition of these bodies to form crystalloids would appear possible and the latter by an increase of size or toxic effect may cause destruction of the parent cell and assume an extracellular position.

Masculinization was present to a greater or

lesser degree in the previously recorded cases of interstitial cell hyperplasia. Small adenoma of these cells have also been described by Berger (1945) and Sternberg (1949), and in these cases masculinizing effects have also been found. The absence of any more definite androgenic effect in our case apart from the facial hirsutism was surprising. It did seem possible, however, that the Brenner tumour may have produced a compensating oestrogenic effect as it is now recognized that these tumours may show hormonal activity (Teoh, 1953; Mackinlay, 1956). It is, of course, difficult to accept that the occurrence of two uncommon conditions in the same patient was entirely fortuitous. However, there would appear no instances in the literature of interstitial cell hyperplasia associated with a Brenner tumour and any definite causal relationship between the two conditions is not obviously apparent.

The evidence at the moment suggests that the hyperplasia of the ovarian interstitial cells is of a primary nature and does not result from pituitary or adrenal stimulation. In those cases where the adrenals have been examined at operation they have been found to be normal and the excretion of 17-ketosteroids has not been raised. This is presumptive evidence against the presence of a primary adrenal masculinizing syndrome. No autopsy reports of such cases are on record.

It is evident that more detailed study of the ovarian interstitial cells in normal and abnormal conditions is required. We would suggest that the term ovarian interstitial cell is preferable to ovarian hilus cell as these cells are clearly the female analogue of the testicular interstitial cells.

Summary

A case of hyperplasia of ovarian interstitial cells associated with a Brenner tumour is described. There was no definite evidence of masculinization. The literature is briefly reviewed.

We wish to thank Miss E. Mills for permission to publish details of this case.

Miss J. L. Perry provided the photomicrographs.

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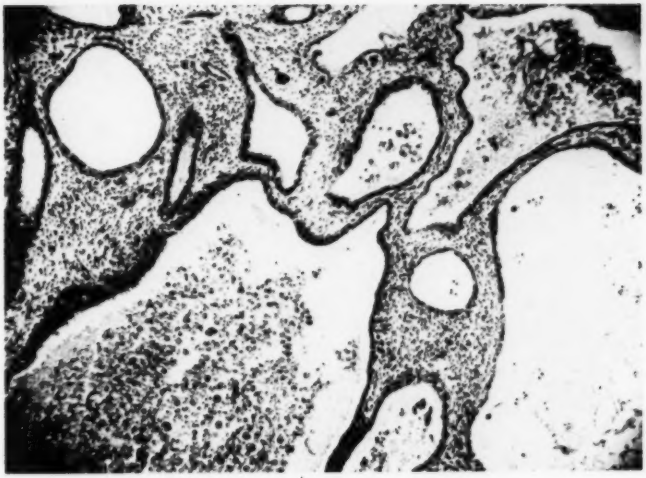

FIG. 1

Benign cystic glandular hyperplasia. Haematoxylin and Eosin. ×65.

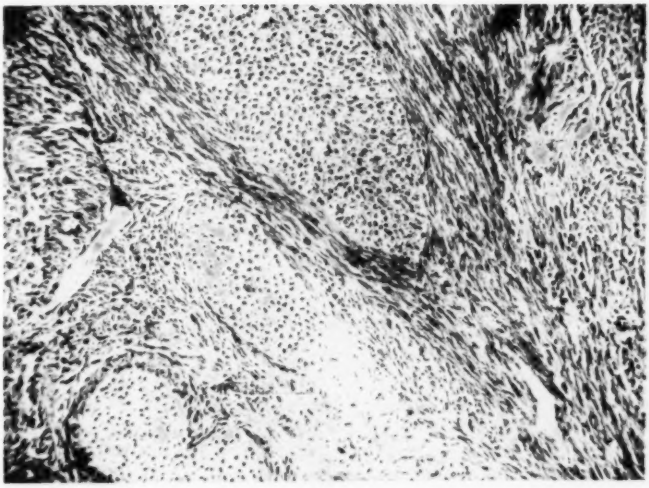

FIG. 2

Brenner tumour of left ovary. Haematoxylin and Eosin. ×85.

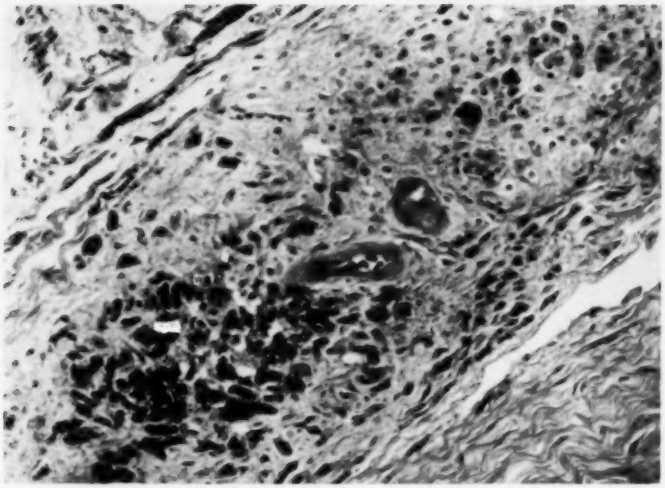

FIG. 3

A large group of interstitial cells. Masson's trichrome. ×125.

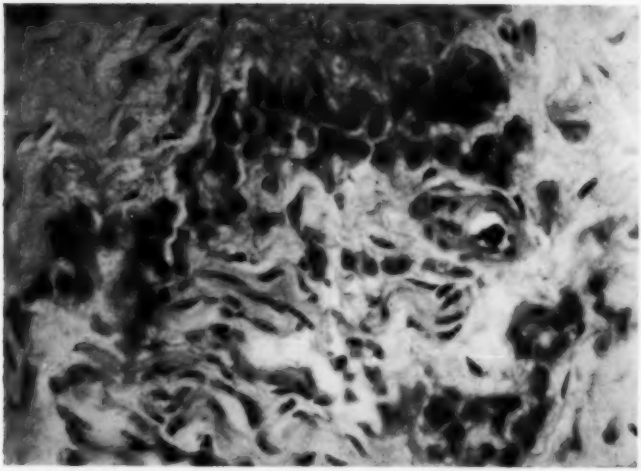

FIG. 4

A group of interstitial cells showing intimate association with nerve fibres. Haematoxylin and Eosin. ×480.

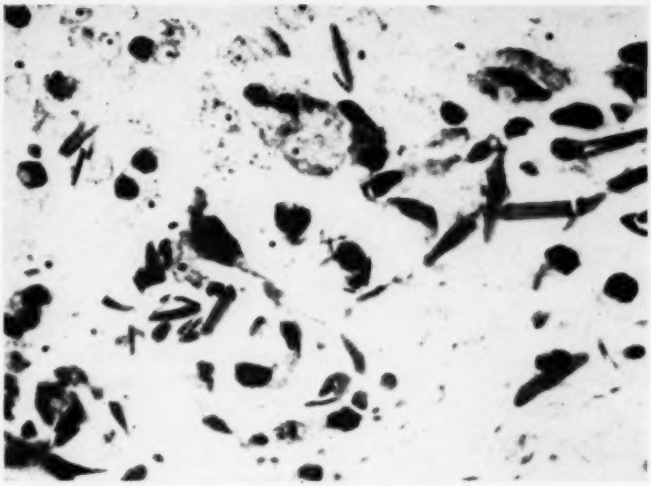

FIG. 5

Crystalloids of Reinke most of which appear extracellular in position. Phosphotungstic acid haematoxylin. ×600.

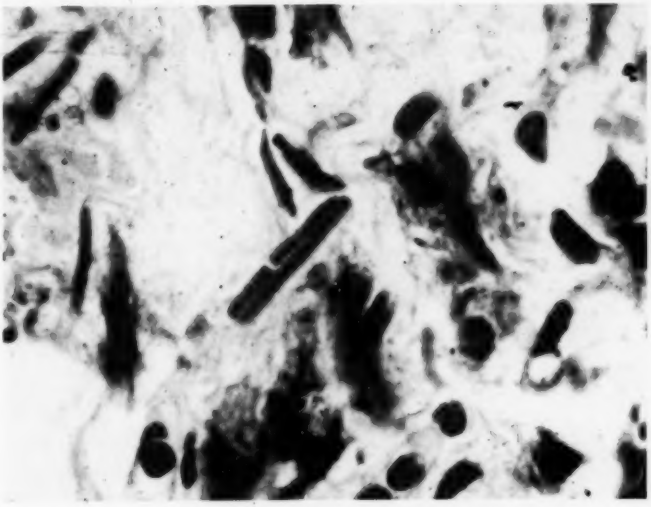

FIG. 6

A Reinke crystalloid showing transverse and longitudinal segmentation. Haematoxylin and Eosin. ×950.

THE DIAGNOSIS OF SUBMUCOUS FIBROIDS BY HYSTEROGRAPHY

BY

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HYSTEROGRAPHY is one of the most valuable methods for detection of uterine fibroids and especially of the submucous variety. This method enables a differential diagnosis to be made between interstitial and submucous fibroids and gives information on the localization and size of the tumour, the distortion of the uterine cavity and other abnormalities. It is thus helpful in enabling us to decide between surgical and non-surgical treatment, and, when operation is decided on, it serves as a guide in the choice of radical or conservative intervention (Zondek, 1939). Of special importance is this decision in cases of sterility or repeated abortions and here information on the patency of the tubes is of considerable value since the decision for conservative surgery in sterile women is dependent upon it.

The diagnosis of submucous myoma is often difficult clinically. Small submucous myomas, when unassociated with other myomas, are difficult or even impossible to diagnose by palpation. In many cases the uterus is small or unchanged in size and diagnosis cannot be made by clinical examination alone. When unassociated with subserous or intramural myomata, profuse and irregular bleeding may suggest a submucous myoma. However, other pathological conditions, such as endometrial polyps, carcinoma of the corpus uteri, functional uterine bleeding and sometimes retention of placental rests, may lead to the same clinical picture. On the other hand, a submucous myoma is not always accompanied by haemorrhage and in approximately one quarter of the cases there is no history of abnormal bleeding.

Duperroy (1952), in a study of the influences exerted by submucous fibroids on menstruation, found that, where the mucosa showed a normal vascular pattern, menstruation was also normal. Cases of menorrhagia or metrorrhagia with recognizable menstruation showed a congestive, atrophic mucosa lying above the fibroid or an ulcerated myoma. The suggestion is made that the atrophic mucosa lying on a submucous fibroid is likely to bleed longer than the surrounding endometrium because of venous congestion and arterial defect, and that ulcerated fibroids might bleed directly into the uterine cavity. Duperroy concludes that the pathological types of bleeding in these cases could be correlated with the structure of the endometrium overlying the tumour, and especially with its vascular pattern. Functional haemorrhage may accompany submucous fibroids; cystic glandular hyperplasia has been found above submucous fibroids.

A submucous fibroid may not be detected despite careful exploration with the uterine sound and curette. The failure of curettage to reveal a tumour is explainable when the submucous fibroid occupies the entire uterine cavity thus forming a false smooth wall which cannot then be differentiated from a normal uterine wall by the operator. Sometimes, even after palpation of the uterus and exploratory incision of the uterine wall at laparotomy, a small submucous myoma may escape attention unless the uterine cavity is opened and digital examination performed. However, submucous myomata can be found by hysterography even among patients without menstrual disorders whose sole complaint is sterility.

TECHNIQUE USED FOR DEMONSTRATION OF INTRA-UTERINE PATHOLOGY

Protracted bleeding, when accompanying such intra-uterine pathological conditions as sub-

mucous fibroids, may interfere with the performance of hysterography, as the procedure is contra-indicated during bleeding because of the danger of leakage of the oil into the open vessels. Another reason for refraining from hysterography during bleeding is the usual presence of blood clots in the cavity which may be mistaken for some pathological condition of the uterus. For this reason bleeding should first be stopped and this is usually achieved by administration of oxytocics over a period of 3–5 days. Such treatment will usually produce uterine contraction and expulsion of clots.

The contrast medium is injected in small amounts before each film is taken. For the first picture, usually 1 to 1·5 ml. are injected slowly under very low pressure. In the presence of a small submucous fibroid with very little or no enlargement of the cavity, this amount will suffice to fill the uterine cavity and to give the best image of the tumour (Rozin, 1954) (Fig. 1). In large cavities additional injections of 1 to 1·5 ml. are necessary in order to complete the filling of the cavum (Hyams, 1935; Rozin, 1954). Figure 2 shows filling of a large uterine cavity containing a submucous fibroid. The contrast medium encircles the tumour more completely with every injection. When the tubes are seen to be filled with dye the procedure is stopped as visualization of the tubes indicates that the whole uterine cavity is completely filled. Incomplete filling of the cavity can lead to erroneous conclusions and thus the procedure should be continued until the tubes are at least partly outlined. Large amounts of contrast medium injected under pressure may overflow and obscure intra-uterine defects by forming a thick layer of dye between the tumour and the uterine wall (Fig. 3).

Films in the oblique position should always be taken as soon as there is evidence of tubal filling and from them more information concerning the size and the position of the tumour can be obtained. Figure 5 shows a large defect due to a sessile fundal tumour. This picture is taken in the oblique position indicating the size and localization of the tumour. The absence, in the oblique position, of a filling defect seen in the antero-posterior position, makes the diagnosis of a submucous fibroid doubtful.

Further diagnostic possibilities are offered by the evacuation (decompression) films taken after the removal of the cannula (Dalsace, 1947; Gérin-Lajoie, 1951; Rozin, 1954). One film is taken immediately after extraction of the cannula, the others in 2 and 5 to 10 minutes later. These films are of special value in cases in which the cavity was over-distended with large amounts of contrast medium, in which the filling defects have partly or completely disappeared (Fig. 3). Often, a defect seen in one film disappears in the next, after the injection of more oil. With the evacuation of a part of the dye previously seen defects reappear and thus reinforce the initial diagnosis. Figure 3 shows a filling defect in the antero-posterior film due to a pedunculated submucous fibroid. The picture is not typical, however, as the amount of oil (3 ml.) overshadows a part of the tumour. Figure 4 taken 2 minutes after removal of the cannula still shows persistence of a round filling defect. Control pictures are taken routinely as usual after 1 and 24 hours.

Characteristics of Submucous Fibroids

The uterine cavity may show slight or no enlargement and distension, depending upon the size of the tumour. The original triangular shape may still be maintained to a greater or lesser degree when the tumour is small (Fig. 1). Larger tumours distort the cavity causing it to assume globular, crescentic or spindle-like shapes (Fig. 2).

According to their type, such tumours may present single, double or multiple nodules. When there is only a single nodule, a very characteristic image is obtained. At the point where the tumour is situated a smooth, rounded, clean-cut filling defect appears in the uterogram. The filling defect is generally regular and circular, and may reach the size of an egg (Fig. 2).

Multiple submucous fibroids, localized in different parts of the uterine cavity, may show separate round filling defects. In the presence of a large fibroid occupying the major part of the cavity with several additional smaller fibroids, the filling defect produced by the former masks those produced by the smaller multiple fibroids.

When the tumour is sessile its attachment to

FIG. 1

Uterine cavity normal in size but with a filling defect in the fundus area, diagnosed as a submucous fibroid. Three previous curettings did not reveal an intrauterine tumour. Histological examination showed glandular cystic hyperplasia of the endometrium. Diagnosis confirmed at laparotomy.

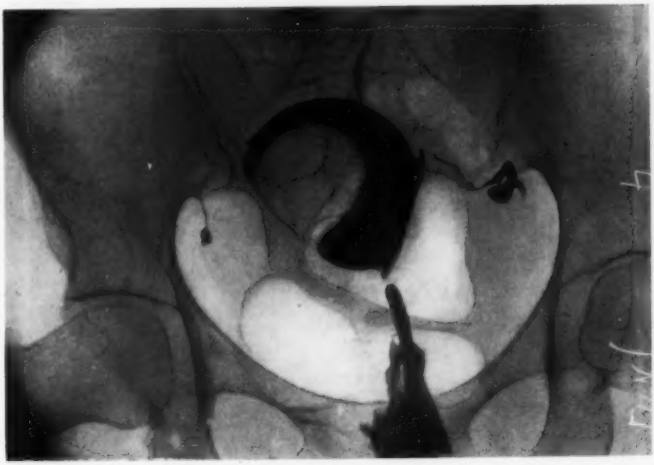

FIG. 2

Film taken after injection of 3·5 ml. Uterine cavity globular. The contrast medium surrounds a spherical tumour. (Sessile submucous fibroid.)

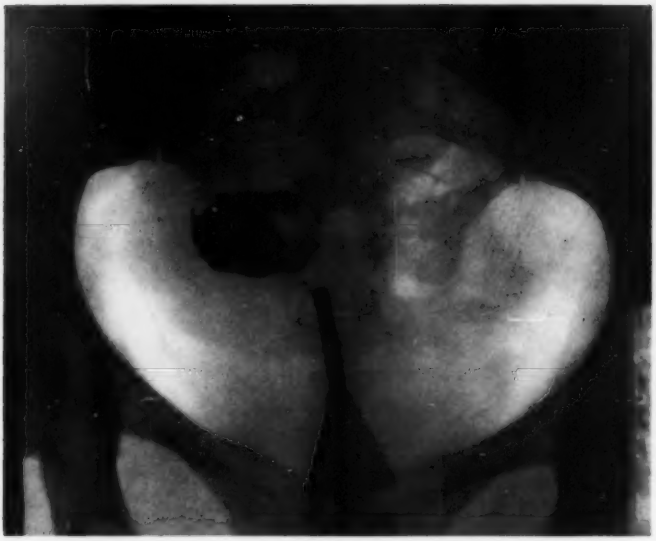

FIG. 3

Pedunculated submucous fibroid. Filling defect occupying a part of the uterine cavity. No characteristic filling defect for pedunculated fibroid as volume of lipiodol too large (3 ml.).

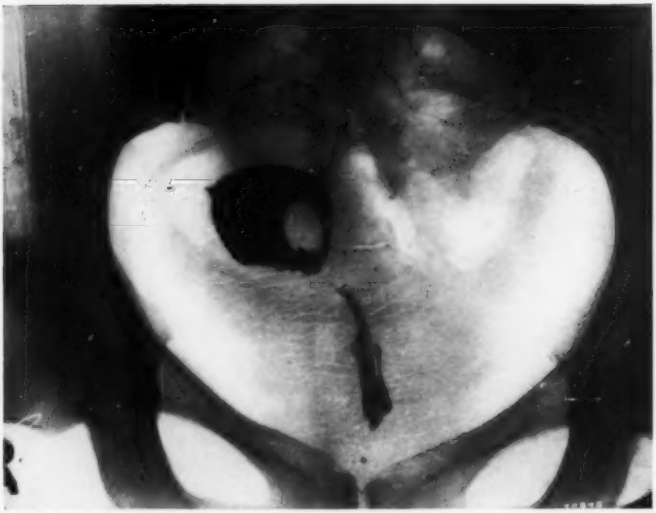

FIG. 4

Post-evacuation film taken after 2 minutes showed a round filling defect.

S.R.

FIG. 5

Right lateral position. Sessile submucous fibroid. Its base is on the fundus. Lipiodol outlines the tumour but not its fundal attachment. Cervix dilated and shortened because of enlargement of the uterine cavity.

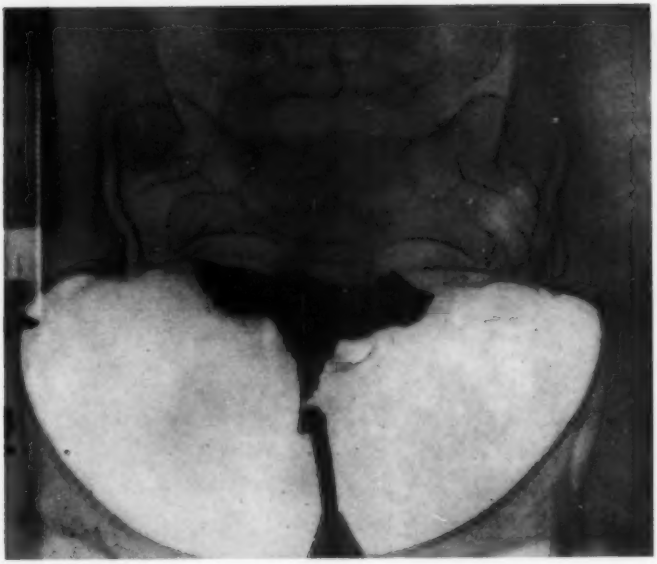

FIG. 6

Uterine cavity enlarged. The semi-lunar translucent zone in the fundal area is due to a fibroid, transitional in type between intramural and submucous.

the uterine wall is characterized by a broad interruption in the outline of the uterine cavity. The filling defect has the more or less regular appearance of the segment of a sphere, incompletely surrounded by contrast medium (Fig. 2).

Pedunculated fibroids are characterized by a lacunar image occupying nearly the whole of an enlarged globular uterine cavity. In some cases, dilatation of the isthmus is also observed. The lacunar image is seen in all the films, anteroposterior as well as oblique. Pedunculated myomas bulge more into the lumen because of their narrow attachment.

A pedunculated submucous fibroid descending into the cervical canal dilates and elongates the cervix. The filling defect, usually large and globular and occupying the whole or a part of the canal, is easily distinguishable from a cervical polyp by its smooth and circular appearance.

Differential Diagnosis of Submucous Fibroids from Other Pathological Causes of Intra-uterine Filling Defects

Endometrial polyps present, in contrast to a submucous fibroid, an irregular shape with uneven surface and accommodate their growth to the shape of the uterine cavity. Difficulty may be encountered in differentiating a pedunculated fibroid from a large polyp since in both conditions the filling defect usually occupies a central position. In general, polyps are elongated, while pedunculated fibroids are circular.

The *transitional form of an intramural fibroid* which is developing toward the cavity does not generally produce the characteristic filling defects seen in submucous fibroids. It produces a pressure defect which only causes contrasts in the density of the shadow of the cavity (Fig. 6). In many cases, however, the differential diagnosis is impossible.

Air defects may simulate small submucous fibroids, the air being injected together with the oil. The air bubbles usually change shape and position in the subsequent films or may disappear completely when additional contrast medium is injected.

Carcinoma of the corpus uteri is generally characterized by a limited filling defect whose outline is more or less irregular and fimbriated (Beclère, 1951). In submucous fibroids the filling defects are generally smooth, regular and circular.

Placental fragments show irregular and fimbriated outlines which may lead to confusion with carcinoma. The diagnosis can be made by curettage. Undisturbed gestation may offer difficulty in differentiation from a submucous fibroid. In these cases the history of amenorrhoea and an Aschheim-Zondek test will usually clarify the diagnosis.

Summary

Uterography is a valuable method for the detection of submucous fibroids because of the difficulty in clinical diagnosis. It makes possible differential diagnosis from other pathological conditions of the uterus. Uterography serves as a guide in choosing the type of operation, radical or conservative.

The technique used for demonstration of intra-uterine pathology consists of the injection of 1–1·5 ml. of contrast medium. In enlarged uterine cavities further injections of the same amount are made and films taken after every injection until visualization of the tubes indicates a completely filled cavity. Too large amounts of dye may overshadow intra-uterine defects. Oblique and decompression films offer improved diagnostic possibilities.

Acknowledgement

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PUERPERAL INVERSION OF THE RIGHT HORN OF A UTERUS BICORNIS UNICOLLIS, WITH A REVIEW OF THE LITERATURE

BY

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THERE are 6 cases of inversion of one horn of a uterus bicornis unicollis associated with pregnancy reported in the literature. The first case was described by Henkel (1905) and the others by Zenela (1935), Bates (1940), Wallau (1941), Sieberts (1950) and Watson (1953).

Details of a seventh case are now presented.

CASE REPORT

Mrs. J.G., age 27 years, was examined on 8th December, 1954, and found to be 10 weeks advanced in her first pregnancy. In the lower third of her vagina, lying in the sagittal plane, was a septum about ½ inch thick, running between the lower half of the anterior and posterior vaginal walls. The only uterine abnormality found at this examination was some deviation of the fundus towards the left iliac fossa.

The pregnancy proceeded normally to term. Labour commenced spontaneously on 21st June, 1955, and proceeded rapidly to the second stage, when the vaginal septum was divided to allow a normal delivery. The third stage was quite normal. The puerperium appeared to be proceeding satisfactorily with the fundus uteri involuting normally, in spite of its deviation into the left iliac fossa. The lochia continued to be fairly heavy and bright red, and, as this persisted on her 14th puerperal day, a vaginal examination was performed to determine its cause. A tumour which bled freely on touch was found to be filling the vagina. It was polypoid, 4 inches in diameter and 5 inches long. It was a soft tumour with a haemorrhagic degenerating surface (see Fig. 1). It was emerging from the external cervical os and its base was attached to the right side of the cervical canal at the level of the internal os directly opposite the internal os of the apparently normally involuting left parturient horn of a bicornuate uterus. The left horn was approximately 5 inches in diameter and the internal os 1½ inches diameter.

In view of these findings and the previous division of a vaginal septum, the diagnosis of inversion of the non-parturient right horn of a uterus bicornus unicollis appeared irrefutable. An examination under anaesthesia followed forthwith to confirm this, to exclude the presence of any retained products of conception in the left horn as the cause of the continued heavy lochia, and to attempt to reduce the inversion.

The previous findings were confirmed by a bimanual examination. A uterine sound entered the single patulous cervix and passed with ease into the left horn to a distance of 4½ inches. The base of the inverted right horn was at the same level as the left internal cervical os and separated from it by the medial part of a small circular muscular ridge 1 inch in diameter, which was surrounding the base of the inversion. Palpable in the right side of the pelvis above the base of this horn was a small tumour which was 1½ inches in diameter and thought to be the right ovary attached to the base of the funnel formed by the inverted right uterine horn.

Manual compression and attempts at digital reposition of the inverted horn caused profuse bleeding, and, as the fundus of the horn felt extremely thin near a minute depression, which was thought to be the intra-uterine orifice of the Fallopian tube, the gentle and unsuccessful attempts at reposition were abandoned. Some retained degenerating membrane was removed from the left horn. As the amount of blood lost during the examination was about 30 ounces, she was given a blood transfusion and a course of Ergometrine was started orally.

On her 23rd puerperal day a bimanual examination showed the left horn was well involuted and the right horn was now only 1½ inches in diameter and 3 inches long. There was only a slight serosanguineous vaginal discharge. She was allowed home to continue breast-feeding of her child and to be observed in the postnatal clinic.

The inverted horn continued to diminish in size and on 20th August, 1955 a salpingogram was attempted

without anaesthesia. The cervical canal was too patulous however and in spite of an attempt to pack the vagina, satisfactory filling of the left horn was not obtained. An intravenous pyelogram showed no renal tract abnormalities.

She was seen on 13th September and involution of the left horn was complete. On 10th October she reported that she was 2 weeks late with her menstrual period when suddenly she had started to lose blood clots *per vaginam*. She was admitted for observation and 2 days later as the bleeding was still very heavy an examination under anaesthesia was performed. The uterine sound entered the left horn to a distance of 3 inches and the internal os was patulous. Curettage produced thick endometrium showing no decidual change. The inverted right horn was 1¼ inches in diameter and 2½ inches long. Its endometrium was bleeding heavily. Manual reduction was impossible. The bleeding subsided in the next 5 days and she was allowed home.

On 29th December she was readmitted with another severe menstrual haemorrhage for which she had to be given a transfusion of 3 pints of blood as her haemoglobin estimation was only 50 per cent of normal. Again, after 5 days, the bleeding had completely ceased.

On 11th January, 1956, under general anaesthesia, salpingography was again attempted. The right horn was still inverted and the cervix was patulous. It was found to be impossible to prevent leakage back into the endocervix and vagina when the acorn nozzle of the syringe was inserted into the similarly patulous internal os of the left horn. Finally, a piece of polythene tubing was inserted into the cavity of the left horn, the internal os of this horn was closed by direct pressure with a finger inserted through the common external os and endocervix, the Neo-Hydriol was injected under direct observation by X-ray screening and the clinical diagnosis confirmed, as shown in Fig. 2.

She had now discontinued her breast feeding and it was decided that on account of her severe menorrhagia and of the irreducibility of the inverted horn spontaneously or artificially, and in order that she might proceed with a normal married life, an excision of the inverted horn should be performed. On 18th January, 1956 at laparotomy the left horn was well involuted and displaced to the left side of the pelvis. Running from the urachus over the bladder and cervix between the two horns to the antimesenteric surface of the upper part of the sigmoid colon was a sagittal plane fold of peritoneum. The right horn was represented by a funnel-shaped depression into which disappeared the right Fallopian tube and the right round ligament. The right ovary was at the mouth of the funnel. Traction was applied to the right round ligament but correction of the inversion was not possible. The constricting ring of the endocervix was plainly visible with the elongated ovarian ligament disappearing into the neck of the funnel. This ring was divided posteriorly as in Haultain's operation and the inversion was now corrected with ease with the aid of a little traction on the right round ligament. The right tube, round ligament and the ovarian ligament were then clamped, divided and tied. The right uterine vessels were similarly ligated. The right horn was then excised from the endo-cervix and this was oversewn in two layers with the stump of the right round ligament sutured to the edges. The two leaves of peritoneum of the right broad ligament were resutured over this bare area enclosing retroperitoneally the ovarian ligament. Haemostasis was complete and the abdomen was closed.

The patient's convalescence proceeded uneventfully and she was discharged from hospital on the 2nd February, 1956. Follow-up since shows she is well and symptom-free.

Inversion of one horn of a uterus bicornis unicollis is an extremely rare cause of vaginal haemorrhage following childbirth. It has been the presenting symptom in all the cases so far described. In 2 of the recorded cases a uterine sound was passed into the normal horn beyond the polypoid vaginal tumour, in the mistaken idea that it was in a normal uterine cavity, and inversion of the uterus was thought to have been excluded by this manœuvre.

In the first 6 cases the inverted horn protruding through the cervix was diagnosed initially as a fibromyomatous polypus and the true diagnosis was only arrived at after excision of the tumour had been attempted or performed. The seventh case is the first to be diagnosed preoperatively and fully investigated before excision. More than half of the cases in which the information is available had an incomplete vaginal septum. No urinary tract investigations were carried out to exclude the possible presence of associated congenital abnormalities except in the present case. Intensive pre-operative investigation of the genito-urinary tract is important so that the operation of choice may be performed for excision of the redundant inverted horn without injury to nearby structures.

All the cases except one were primiparae and only one breech presentation is recorded.

There were no symptoms suggestive of an acute uterine inversion in any of the series and the earliest case discovered was on the second puerperal day (Watson, 1953), whilst the latest was 18 months after delivery (Henkel, 1905). The 5 most recent cases have all been discovered within 24 days of delivery.

The gravid horn was on the left in 3 instances, on the right in 2, and no information was available in the other 2 cases. It is of great

interest to see that in 4 cases, and probably also in Bates's case, the inversion occurred in the non-gravid horn. It is in these 5 cases only that the information is available.

Two patients were treated with ecbolics for primary uterine inertia and both of these cases and one other had Credé expression of the placenta.

The lack of complications and haemorrhage found after simple vaginal excision of the inverted horn in 2 cases is impressive. Three other undiagnosed causes where this method was being used required a laparotomy in 2 and a colpotomy in the third.

The left internal cervical os in the present case was dilated sufficiently to admit the tips of three fingers with ease on her fourteenth puerperal day. The large dilated endocervix and patulous external cervical os easily admitted three fingers and the cervical canal was three inches long. Presuming the circular ridge around the base of the inverted horn marked the boundaries of the right internal cervical os, this was similar in diameter to that of the opposite side, and possibly sufficiently dilated to allow complete inversion of the smaller horn to occur with an increased intra-abdominal pressure such as straining with defaecation or coughing.

Summary

A seventh case of puerperal inversion of one horn of a uterus bicornis unicollis has been described. It was diagnosed and investigated pre-operatively.

Manual reposition failed but an opportunity for spontaneous correction to occur was allowed without success. Severe menorrhagia demanded treatment which consisted of excision of the inverted uterine horn by the abdominal route.

The relevant available details of the other 6 cases are summarized. It is suggested that the inversion is due to an incompetent internal cervical os and a patulous cervical canal in which the relatively small non-parturient horn is finally inverted when there is a sudden increase of intra-abdominal pressure as in straining or coughing.

We wish to thank Mr. John W. Mitchell for the photographs.

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FIG. 2

Uterosalpingogram showing the left horn and tube of the uterus bicornis unicollis filling normally with opaque fluid. The polythene tubing is seen and the X-ray shows the index finger occluding the os of the left horn. Below the tip of this finger is seen the opaque fluid outlining the inverted horn in the vagina.

FIG. 1

The healing stump of the vaginal septum divided at the time of delivery is shown just below the urinary meatus. Almost filling the vagina and visible immediately on separating the labia majora is the inverted right hemi-uterus with its friable bleeding degenerating endometrium.

PSEUDO-OSTEOMALACIA

Report of a Case

BY

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OSTEOMALACIA is a rarity in this country and, while obstetric textbooks frequently contain radiographs of a tri-radiate pelvis, the condition is seldom seen. We are indebted to Maxwell (Maxwell, 1923, 1930, 1947; Maxwell and Miles, 1925) who described in detail the condition as it occurred in China.

Since Lambert in 1700 (Ribémont-Dessaignes and Lepage, 1894) reported the first case in Europe, sporadic cases have occurred especially in the Rhine Valley, Switzerland and Hungary, and in times of famine when calcium and vitamin D intake are reduced. Dalyell and Chick (1921) reported hunger osteomalacia in Vienna following the Great War and in this country Bulmer (1935) traced 12 cases and further cases have been reported by O'Donovan (1939), Kenny (1941) and MacLennan (1944).

Osteomalacia must be distinguished from pseudo-osteomalacia in which the characteristic pelvic deformity is produced in hyperparathyroidism, idiopathic steatorrhoea, renal osteodystrophy, senile and thyrotoxic osteoporosis and fracture of the pelvis. Baird (1955) illustrates a case of osteitis fibrosa cystica causing a pelvic deformity similar to osteomalacia.

Both Bulmer (1935) and Maxwell (1947) stress the difficulty in diagnosis of sporadic cases of osteomalacia in this country and its differentiation from pseudo-osteomalacia.

CASE REPORT

Mrs. D.C., aged 23 years, was first seen at the 11th week of her first pregnancy. She had never travelled abroad and was a Londoner, except for the war years 1939 to 1942 when she lived in Surrey. As a baby she was breast fed for three months and easy to rear. Though of small stature, she sat up and walked at the usual age and played games normally at school. Her teeth erupted at the expected times and were healthy. No illnesses of note occurred in childhood and there was no history of rickets or renal or gastro-intestinal disease; tetany and muscular cramps had not occurred. Her family were economically secure and food was plentiful. At 16 years of age transient pain occurred in her left hip; it lasted for a week and was attributed to "rheumatism"; it was not severe and did not limit her physical activity. At no time was there pain in her pelvis or legs.

On examination this patient weighed 108 pounds and was 5 feet 2 inches tall. Her urine contained no albumen and her haemoglobin was 88 per cent. Her teeth were healthy, her limbs straight, and there was no chest deformity or other evidence of childhood rickets. There was no thyroid enlargement or evidence of thyrotoxicosis. The pubic symphysis projected forward as a beak and the ischio-pubic rami were parallel, markedly reducing the pelvic outlet, and making vaginal examination difficult.

Radiological pelvimetry at the 35th week of pregnancy showed a tri-radiate pelvic brim with approximation of the acetabulae (Fig. 1). The sacrum was well hollowed with forward displacement of its second segment (Fig. 2) and the pelvic outlet was extremely small with inturning of the ischial tuberosities (Fig. 3). The pelvic measurements were as follows: conjugate, 4·3 inches; transverse brim, 3·3 inches; available transverse brim, 1·2 inches; A.P. mid-cavity, 5·0 inches; ischial bi-spinous, 1·9 inches; A.P. outlet, 5·3 inches; inter-tuberous, 2·0 inches; subpubic angle, 30 degrees. Radiological examination of both pelvic and limb bones showed good differentiation between cortex and medulla with normal bone density and there was no suggestion of any active bone disease.

An elective Caesarean section at term was planned. Throughout the pregnancy this patient remained well; vitamin supplements were prescribed and taken and no pain or discomfort was experienced in the pelvis or legs. At the 38th week she was admitted in strong labour having felt no foetal movements for the preceding two days. There was no evidence of pre-eclamptic toxaemia, the foetal heart was inaudible and the foetal head was not engaged. Lower segment Caesarean section was performed, since craniotomy was considered a hazardous procedure in such a grossly contracted pelvis, and a macerated stillborn female infant weighing 4 pounds 5 ounces was delivered, followed by an infarcted placenta weighing 11 ounces.

No cause was found for the intra-uterine death and the infant showed no evidence of foetal rickets. The subsequent puerperium was uneventful.

Four months later the patient became pregnant for the

second time. At the 38th week of an uneventful pregnancy, elective lower segment Caesarean section was performed and a healthy male infant weighing 5 pounds 2 ounces was delivered. The baby thrived and the puerperium was uneventful.

Biochemical estimates of the mother's serum calcium and phosphorus and phosphatase were within normal limits, i.e., serum calcium 10·2 mg. per 100 ml. (normal 9–11); serum phosphorus 3·1 mg. per 100 ml. (normal 2·5–3·5); and serum alkaline phosphatase 11 units (normal 4–14).

Family History

Mrs. D.C., was the fifth of 6 siblings. Her mother was delivered of her first and sixth children, both weighing 9 pounds, by obstetric forceps. Her second pregnancy ended in a stillborn breech delivery and her remaining pregnancies were normal. Radiological pelvimetry was performed on the mother of Mrs. D.C. and revealed a large gynaecoid pelvis.

Discussion

The clinical features of osteomalacia are too well known to require amplification, its onset being heralded by pain in the lumbar region and thighs. This aching pain is intermittent but characteristic and to the Chinese patient the disease goes under the name of "Yao T'ui T'eng" or "back and thigh pain" (Maxwell and Miles, 1925). The case reported here had fleeting pains in the left hip at the age of 16 years, and, though osteomalacia may occur at puberty, it is difficult to believe that such a gross degree of pelvic deformity was accompanied by such trivial symptoms.

The cause of the pelvic deformity in this case must remain obscure, for no active bone disease was in progress whilst this patient was under observation and her history (obtained from both the patient and her mother) was unenlightening. Her "osteomalacic" pelvis is either due to a congenital abnormality or has resulted from an undiagnosed childhood steatorrhoea preventing the absorption of vitamins and calcium. The deformity is so extreme, and so localized, that a local rather than a general cause is likely and the former theory is favoured.

Summary

A case of pseudo-osteomalacia is described of unknown aetiology.

Acknowledgments

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FIG. 2
Lateral view.

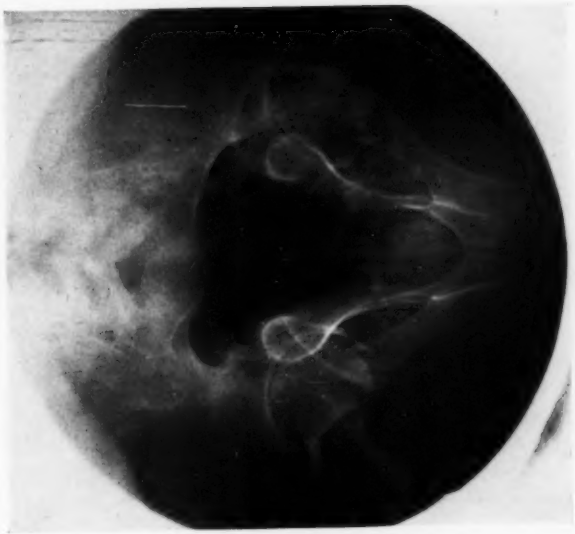


FIG. 1
Brim view.

D.S.

FIG. 3
P.A. view.

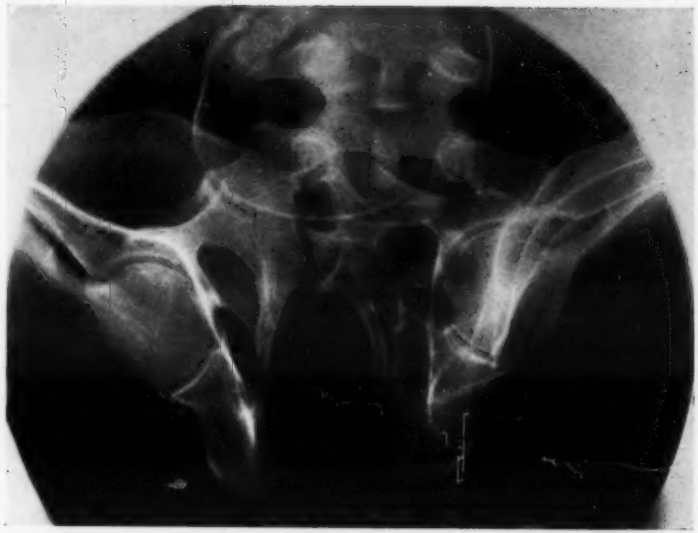
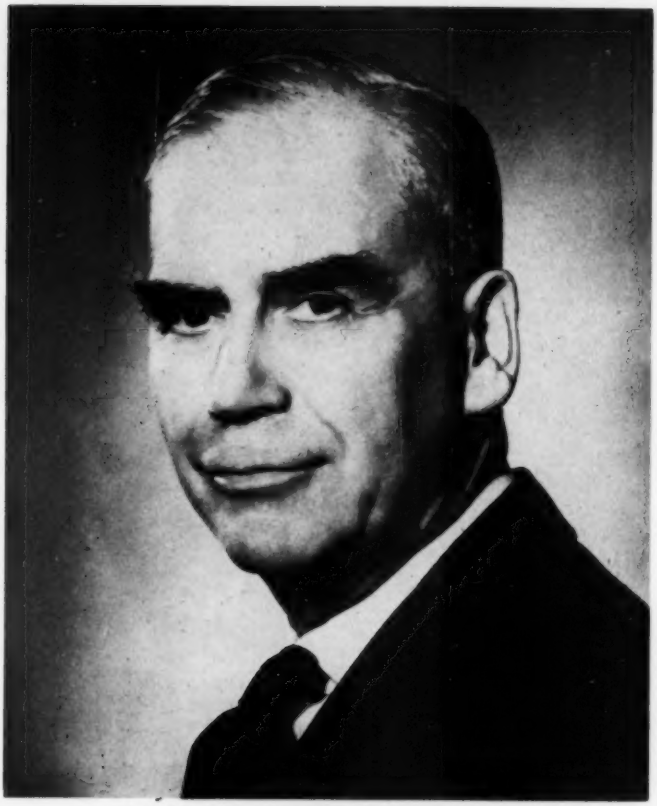


FIG. 4
Outlet view.



SIR WILLIAM GILLIATT

Obituary

Sir WILLIAM GILLIATT

K.C.V.O., M.D., M.S., F.R.C.P., F.R.C.S., F.R.C.O.G., Hon.M.M.S.A.

THE sudden and tragic death of Sir William Gilliatt in a motor accident on 27th September has robbed Obstetrics and Gynaecology of a trusted and outstanding personality of this generation. Although 72 years of age he appeared much younger and showed every evidence of having a great contribution to make for many years ahead.

He was born in Boston, Lincolnshire. His father, who opened a chemist's shop there, died when he was young, but his mother carried on the business and sent her son first to Boston Grammar School and later to Wellingborough College. His appointment as a prefect marked him as showing early powers of leadership.

He entered the Middlesex Hospital Medical School in 1902 and had a brilliant student career winning the Hetley Clinical Scholarship, the Leopold Hudson Scholarship, the Junior Broderip Scholarship and the Lyell Gold Medal. In taking his M.D. London he was again awarded a gold medal.

Gilliatt had a brilliant career as student, resident and registrar at the Middlesex. During this time he was house surgeon to Sir John Bland-Sutton. At the celebrations of the centenary of the birth of Sir John, Gilliatt, in the course of his remarks, pays tribute to the inspiration that Sir John gave him. Gilliatt says that what he remembered most was "that you could not fail to learn from him". Incidentally Gilliatt reveals how the great man of that day recognized with kindness the ability and devotion of the young man to the service of his patient. A patient was admitted who had tried to commit suicide with a revolver shot. Gilliatt assisted Sir John at the operation and spent many hours in the after care of the patient, who recovered. Just before the patient was discharged from hospital Sir John gave a clinical lecture on the case. At the end of his talk the lecturer said "My house surgeon worked hard and saved the man's life, for which I am giving him a gold watch". Gilliatt greatly treasured this watch.

In 1916 he was appointed to the staff of King's College Hospital. He served on the staff of several other hospitals and at the time of his death was consulting surgeon to King's and to the Samaritan Free Hospital for Women.

Although Gilliatt was known to his obstetrical and gynaecological colleagues as outstanding for many years he came into the public eye when he attended Her Royal Highness the Duchess of Kent for her three children, and when he attended Her Majesty the Queen (then Princess Elizabeth) for the births of the Duke of Cornwall and Princess Anne. When Her Majesty came to the throne he was appointed Surgeon-Gynaecologist to her.

Many honours were bestowed upon him. He was created C.V.O. in 1936, knighted in 1948 and created K.C.V.O. in 1949. These honours sat easily upon him and, in spite of, indeed perhaps, because of, his services to the highest in the land he never "lost the common touch".

The foregoing brief survey of such a wonderful career gives little knowledge of the man and his numerous activities and interests.

He threw his whole heart into anything he undertook. He had great ability in weighing up any problem and once he had made up his mind expressed himself lucidly and shortly with due regard for the feelings of others. In consequence he made a contribution to the work of any Committee on which he sat. King's College Hospital, its welfare, progress and good name were ever in his mind. He was elected to the Committee of Management in 1932 and was

very pleased when he was appointed Vice-chairman in 1945 whilst still an active member of the staff. With the advent of the National Health Service he became a member of the Board of Governors and was appointed Vice-chairman and Chairman of the Nursing Committee. He took great interest in the affairs and welfare of the nursing staff and this not only in his own hospital for he was Chairman of the Professional Nurses and Midwives Conference.

Gilliatt gave great service to the Royal College of Obstetricians and Gynaecologists. He was a Foundation Fellow and was first elected to Council in 1932. He held office with distinction as Acting Hon. Secretary, Hon. Treasurer and President. By his wisdom, his devotion to the duties of his office and his accessibility he greatly helped to establish the high place which the College holds in medical affairs. To many Fellows and Members, including a large number from overseas, his kindness and hospitality will be a treasured memory.

It was fitting that a number of important events in the annals of the College occurred during the years of his Presidency (1946–1949). The Royal Charter, delayed by the war, was granted in March, 1947.

A year after the birth of Prince Charles, Their Royal Highnesses the Princess Elizabeth (as she then was) and the Duke of Edinburgh attended the annual dinner. Her Majesty Queen Elizabeth (now the Queen Mother) graciously accepted the office of Patron of the College at this time and in November, 1949, visited the College to receive the Honorary Fellowship. There can be no doubt that these evidences of Royal approval were, in no small measure, due to the service which Gilliatt had rendered to the Royal family.

In 1947 Gilliatt launched an appeal for funds to build a new College house. He worked hard to make this a success and was himself a very generous donor.

Two other activities related to medicine must be mentioned. He was a Liveryman of the Worshipful Society of Apothecaries and served on its Court of Assistants from 1949 to 1956. When he might have been expected to reduce his activities he accepted the Presidency of the Royal Society of Medicine for 1955 and 1956. He filled the office with distinction and worked very hard for the Society in a difficult period.

As a clinician and consultant he set himself the very highest standards; nothing less would satisfy him. He was a painstaking and able diagnostician, his judgment was very sound and no point was too small in the care and welfare of his patients to escape his notice and attention. Naturally his patients in private and in hospital were devoted to him.

As a teacher he was simple, lucid and somewhat dogmatic. He was at his best in the out-patient department or at the bedside. His habit of asking questions of the students who gathered round him may have frightened the poor or lazy ones but those who gave evidence of working and trying hard were given great encouragement by him.

From house surgeons and registrars he expected the same high standard he applied to himself. Any slackness received biting reproof but honest endeavour was always recognized by the greatest help and encouragement.

Gilliatt had an innate shyness and reserve and, in spite of all the honours which came his way, a real humility. These characteristics led some to think him aloof but this was far from the truth. He was a most friendly man, not shown in the modern way by the easy use of christian names, but in a deeply genuine way. This friendship was not lightly given but once accepted into his large circle the kindnesses received were incalculable.

His hobbies were golf and racing, especially at Ascot. His last afternoon was spent at Ascot and those who saw him there say he had a happy and enjoyable time; then the end came swiftly, as he would have desired it.

Those of us who were privileged to know his family life realize however what a shattering blow it was to the family. He and his wife were so truly part of each other and helped each other in so many ways.

To Lady Gilliatt, his son and daughter we extend our deepest sympathy.

ARTHUR A. GEMMELL.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of the Council was held in the College House on Saturday, 24th November, 1956, with the President, Mr. Charles D. Read, in the Chair.

Dr. Edward White of Melbourne was appointed to give the William Meredith Fletcher Shaw Memorial Lecture for 1957.

The following were appointed *Leverhulme Research Scholars* for 1957:

J. Naylor Hunt and F. A. Murray (jointly), London,
N. F. Morris, London.

The following were appointed *Bernhard Baron Travelling Scholars* for 1957:

D. Methuen, Oxford and G. P. Charlewood, Johannesburg.

The *William Blair-Bell Memorial Lecture* for 1957 was awarded to Claud W. Taylor, Birmingham.

The *Green-Armytage Short-Term Travelling Scholarship* for 1957 was awarded to C. A. Simmons, London, and the prize for an essay on "Methods for improving the results of forceps delivery" awarded to J. Mann, Toronto.

The following was admitted to the **Membership:**

Wunnava Saroja Ramarao.

The following have been awarded the **Diploma in Obstetrics:**

Robert John Wallace Adamson.
Philip Graham Allen.
Anne Allison.
David Frederick Ashton Aubin.
John Derek Avison.
Neville Martin Bailey.
John Godfrey Ball.
Irene Lorraine Barbour.
Elizabeth Shirley Millard Barnes.
Margaret Alston Barrie.
Geoffrey Baum.
Norman Lawrence Beisley.
John Allen Benbow.
Geoffrey Bennett.
Dennis Brian Beveridge.
Vijaya Popatlal Bhoopatkar.
George Alan Christie Binnie.
Jane Isabel Kennedy Binnie.
Paul Byrne Biddell.
John Scrivener Birch.
Eric Sutton Blackadder.
Suzanne Burton Blackburn.
George David Blackledge.
Kevin Godfrey Bland.
Peter Owen Bodley.
Alfred Peter Bolt.
John James Bowen.
Kenneth William Brewster.
Isabel Kate Elizabeth Brister.
Bernard James Brooks.
Peter Harold Browne.
Gillian Mary Bryant.
Denys Charles L'Estrange Burges.
John Burgess.
Patricia Burne.
Helen Maclean Caldwell.
William Harte Callander.
William MacDowell Campbell.
Geoffrey Richard Charles Campion.
John Denys Campling.
Lawrence Martin Carter.
John Brian Chapman.
Aileen Percival Cherry.
David Ruston Childs.
Margaret Anne Clark.
Robert West Harrison Clarke.
Keith Anthony Clare.
Robert Cameron Cochrane.

Ronald Wilson Coffee.
Sydney Cohen.
John Burton Cole.
Anthony George Collington.
Peter Cook.
Wendy Ann Cook.
Reginald Bruce Conyngham.
John Court Cornwell.
Patricia Josephine Mary Cotter.
Iain Dudley Stuart Cowie.
Peter Seymour Virgil Cox.
Rehemat Mohamedhusein Curmally.
Patrick Bartholomew Curtis.
Kathleen Elizabeth Coulter.
Kenneth John Dalgliesh.
Christine Mary Davidson.
Michael John Abbott Davies.
Rhys Glynn Davies.
John Lydford Davis.
William Goodhugh Dawson.
Gordon Thomson Day.
Kenneth Gordon Dickinson.
John Hugh Dickson.
John Michael Hill Dickson.
John Reid Duke.
Peter George Dunbar.
William Dunn.
Ronald Arthur Eames.
Aloysius John Edwards.
James D'Arcy Edwards.
John Raymond Edwards.
Marian Searby Edwards.
Jacob Joseph Eisenberg.
Carice Ellison.
Anthony John Entwistle.
Maureen Etchells.
Bruce Harry William Finlaison.
Freda Williamson Fleming.
Phyllis Mary Fleury.
Joseph Roy Flury.
Frank David Chubb Ford.
Peter Hardwick Foote.
Denis Byron Fowler.
Robert Neil Galloway.
Frances Elizabeth Garrad.
Michael Christopher Guard.
Grace Margaret Gee.
Bridget Maud Gell.
Janet Goodall.
Joan Tinning Graham.
Malcolm Arthur Holmes Graham.
John Michael Silvey Grieve.
Ian Michael Guiver.
Mureen Ethel Hall.
Guy Harris.
Kathleen Muriel Harrison.
Margaret Ann Hatton.
Alan Haworth.
Robert Walker Henderson.
Patrick James Gerard Henry.
Ralph Stuart Tremearne Hey.
Rosemary Ann Hill.
Doreen Elizabeth Hillier.
George Harold Hilton.
Kenneth Ian McKenzie Hogg.
Brian William Holbrook.
John Brendan Holland.
George Michael Robert Holliday.
Streamlet Hooroo.
Verna Patricia Houghton.
Alan Justin Greenway Howse.
Mary Howson.
Elizabeth Anne Hudson.
John Hughes.
Barry Ingham.
Uriah Jacobson.
Bernard Francis Jamison.
John Ward Jenkins.
John Morris Jones.
David Harold Jones.
Peter Morgan Newton Jones.
Khorshed Sorabji Karai.
William Gillespie Kilpatrick.
Alan Keith Knowles.
Anthony Henry Labrum.
Brian William Laithwaite.
Vincent Leach.
Gillian Alison Lomax.
George Earle Lovatt.
Ian Vincent Longfield.
Eileen Mairi Maccoll.
Duncan MacGregor.
Angus Mackay.
Eric Joseph Barry McArthur.
Peter Desmond Patrick McGrath.
Allan Gordon Walker McLeod.
Lawrence Alexander McMichael.
Robert Buchanan Macpherson.
Santosh Madan.
Frederick Millward Mansfield.
Anabel Jane Maud Mason.
Denis Thorpe Mathews.
David Henry Mathias.
Michael Kenneth Mead.
Herbert Augustine Harcourt Melville.
Anne Diana Micah.
Thomas William Paul Millar.
John Hugh Mitchell.
Peter James Mitchell.
Wendy Lilian Mitchener.
Rafiqa Ghulam Mohammad.
Philip Conway Moore.
John Mather Morfitt.
John Thomas Fowler Morrall.
James Charles Muir.
Ian Campbell Murison.
Colin William Angless Murray.
Albert Gunaratnam Muttuthamby.
Margaret Nathaniel.
James Hall Naysmith.
David Arthur John Neden.
Michael Richard Newell.

Wendy Elizabeth Noble.
Francis Brian O'Connor.
Colin Blackwood Officer.
David Bruce Rowan Osborne.
William John Houston Paradice.
Jyoti Anilkumar Parikh.
Francis Bruce Wyndham Parker.
Richard Henry Oxlade Parker.
Kantilal Laxmichand Parmar.
James Dennis Parry.
Muriel Parsons.
Upendra Nath Pathak.
Peter Robert Bradley Pedlow.
Marguerite Eleanor Pennefather.
Ugo Neil Phillips.
John Ferguson Pritchard.
James Roger Raby.
Michael Bruce Raby.
Madan Mohan Rana.
John Nicholas Rea.
Rolf Carlton Richards.
Thomas Martin Richards.
Nathaniel Rifkind.
Andrew Robertson.
Ian Hardy Robinson.
Margaret Reynolds Robinson.
Robert Bruce Stuart Ross.
Terence John Frood Rockey.
Maurice Jacob Samuels.
Michael Burbridge Scott.
Madhukanta Krishnalal Shah.
Rita Winifred Shannon.
John Leonard Hughdeburgh Sharp.
Ma Khin Si.
David Ward Smith.
Robert Ward Smith.
David Glyn Standing.
Paul Steward.
Angela Margaret Strahan.
Rhona Stringer.
John Lionel Vickery Summerhayes.
Hilary Kathleen Cranleigh Swash.
Geoffrey William Tamlyn.
Charles Murray Taylor.
Roy Charles Taylor.
Thomas Taylor.
Sarosh Meher Thanevala.
Glenna Thomas.
Lionel Edgar Thomas.
Frances Celia Thomson.
Anthony David Thurz.
Elizabeth Mary Tilsen.
Ronald Stanley Todd.
Edward James Turner.
John Turpin.
Mary Monica Tyndall.
Anthony Seymour Valentine.
George Richard Vesey.
Jean Margaret Walinck.
Oswald Heath Watkins.
Colin Watson.
Martin Bertram Watts.
Tilak Ananda Weerasuriya.
Peter George Wells.
Frederick Laurence Whalley.
Peter Hans Wiesendanger.
Margaret May Wilcox.
Barbara Mary Williams.
Hilary Frances Williams.
John Pyers Mostyn Williams.
David Watson Williamson.
James Herbert Patrick Willis.
Robert Geoffrey Bainbridge Willis.
Philip Kenneth Wilson.
Sheila Alice Wood.
Mary Beryl Woodfield.
Donald Pierpoint Woods.
David Bellamy Wooldridge.
Geoffrey Henry Worsley.
Ian Wort.
Henry William Wright.
Joan Lilian Young.
Stuart Shepherdson Young.
George William Golder Yule.

REPORTS OF SOCIETIES

GLASGOW OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

April 1956

The Seventh Meeting of the Glasgow Obstetrical and Gynaecological Society was held on Wednesday, 18th April, 1956, in the Royal Faculty of Physicians and Surgeons, 242 St. Vincent Street, Glasgow. The President, Dr. H. R. MacLennan occupied the Chair.

The main business of the meeting consisted of four short papers by Dr. Charles P. Douglas, Dr. Ian Macdonald, Dr. Andrew W. Laughland, and Drs. Donald F. Bruce and Archibald Dick. The article by the last-named authors appears at page 884.

Gynaecological Surgery in the Elderly

By Dr. Charles P. Douglas, Victoria Infirmary, Glasgow

In Great Britain today we have an ageing population, which means that more and more elderly people will require medical treatment. In view of this it was felt that it would be worth while reviewing the treatment of elderly patients in the Gynaecological Department of the Victoria Infirmary, Glasgow. There is a tendency nowadays to say that the treatment of old persons is best left to those who specialize in gerontology. But, as gynaecologists, we feel that it is not necessarily so, and that we have a lot to offer such people. Such an offering is not necessarily to save life, but is often for the purpose of relieving disability, which in some cases is almost as important. We have to remember that women seldom retire, and their health is needed even for baby-sitting. And, in addition, we can help greatly to prevent the older persons from being a burden on the younger.

There are many people who are virtually disabled by such conditions as genital prolapse, who are invalids solely because there is a poor realization of the possibilities of treatment today. This lack of perception appears sometimes to operate on three levels, the specialist, the family doctor and the patient. There is too often a general feeling that, as it doesn't shorten life, it doesn't warrant active measures. But surely the point is that although it may not shorten life it vastly shortens useful life. There is a tendency to say "let them live in peace", but that is tantamount to saying "let them live in pieces".

Although old age pensions are drawn at 60 we felt that clinically the stigmata of old age do not appear so early, and therefore we took 65 years as our lower limit. The Life Table obtained from the Scottish Life Offices shows that the expectation of life in the elderly is, perhaps, surprisingly long; even at 70 it is 10 years. Although at 75, when the expectation of life is 7 years, much radical surgery is probably too great a risk, if the lady is in her mid-sixties, with 13 years or so to live, radical treatment is both possible and valuable.

In the last 5 years we have operated upon 163 persons of 65 years and over. It is interesting to compare this with the number operated on 20 years ago. Although the total number of admissions has almost doubled, the relative numbers of the elderly have increased almost fourfold; the number operated upon has also risen fourfold, but in major operations it is almost 5 times as many.

There were seen at the out-patient department 231 patients of over 65 years. Operation was advised in 198 and only 4 refused this; 194 were admitted and operation was carried out in 163 of these, the remainder being treated by other methods. Of course, the true rate of operability in such patients is not known, partly because many still do not present themselves, and many other factors influence treatment. It is, however, obviously high, and it is important to find which patients can be operated on and those who must be refused operation, and why this is so. The diseases associated with old age actually interfere very little with treatment. The main contra-indications to operation are cardiac disease, senility and frailty. Hypertension is relatively unimportant.

When operation is to be carried out, a few simple precepts should be observed. The essentials are rest and adequate nourishment. We feel that these patients should have about 7 days in hospital before operation. This allows the complete assessment of fitness, with enlistment of the services of other specialists for advice, although we find in practice that this is seldom needed as most of their complaints are of a simple nature. It also allows observation by the nursing staff of the patient's degree of activity, and the necessary rest before undergoing a physical ordeal. Nourishment is also essential, as good diet before operation often saves much post-operative biochemical upset. This, of course, entails a rather longer stay in hospital than with younger patients, but we feel that this is fully justified. The average stay in hospital is about one month.

Post-operatively the patients are asked to undergo a moderate regime of early ambulation, not with a view to allowing them home early, but really to keep the patient's activity at a reasonable level. When confined to bed, these elderly patients may very rapidly become inactive and rehabilitation can then be very slow. When the operation is performed, we feel that there are two main principles to be followed. Firstly, that the simplest procedure which will ensure adequate treatment should be performed. Secondly that the operation should be performed as speedily as is feasible. In fact, we feel that speed is an essential; in our experience, if the operation

should take more than an hour, there is a rapid deterioration in the condition of the patient.

The anaesthetic used in these cases is left to the discretion of the anaesthetist concerned. That mainly used has been soluble Thiopentone induction with the usual inhalation maintenance and with a relaxant if necessary. There would appear to be no place for hibernation anaesthesia in these cases, as the degree of shock occasioned by these operations is not great and the time factor is short.

These operations, which included almost all the standard gynaecological procedures short of radical extirpation for carcinoma, show a mortality of 3·5 per cent. There were 4 deaths and none followed a minor operation. The oldest patient who underwent a major operation was 82 years of age. There were 7 aged 75 or over and 31 aged 70 or over.

It is our practice to follow up these patients for about 6 months, and then if they are fit and well they are dismissed. If, however, they have had a carcinoma or there is other good reason for continuing to observe them, they are followed up for a longer period. Sixty-nine of our patients were dismissed well after 6 months. A further 29 were well at least 2 years after the operation. There was one recurrence of prolapse after 3 years and we know of 7 patients who ultimately died of a carcinoma, who had at least 2 years of good health in the interval. We have no evidence of progress from 5 patients.

Despite the operative mortality which might be considered a little high, the success of operation taken together with the reasonably good results at the follow-up clinic, suggest that it is well worth while treating the elderly gynaecological patient when such treatment is necessary. We feel, therefore, that there is a large number of women who, if they are made aware of the possibility of treatment, can approach an impending operation with a reasonable assurance that the results will be beneficial.

Hodgkin's Disease in Pregnancy

By Dr. Ian Macdonald, Western Infirmary, Glasgow

Since Hodgkin's disease and the reticuloses generally are diagnosed more frequently and earlier in their course nowadays than they were 20 or 30 years ago, and since more efficient radiotherapy and chemotherapy are available, the association of Hodgkin's disease and pregnancy is less rare than it used to be. Thus we encounter more often the problems of the management of these cases. The early literature on this subject refers mainly to severely ill patients, the diagnosis often being made post-mortem.

Myles (1955) analyzed all reported cases very fully. His deductions are, however, open to the criticism that they are not based on the whole story. He gives the incidence of Hodgkin's disease in pregnancy as 1 in 6,000 deliveries. It is thus twice as common in his series as it has been at the Royal Maternity Hospital, Glasgow, during the past 8 years. Either his series is a selected one, or we are not making the diagnosis as often as we should.

In the evaluation of the effect of pregnancy on Hodgkin's disease, the exacerbation or relapse rate in the latter during pregnancy is shown quite convincingly by Myles (1955) to be no higher than the relapse rate one would expect in a non-pregnant woman with Hodgkin's disease over a 9-month period (50 per cent). This concept is a most useful one and was first enunciated by Kasdon (1949). Since pregnancy does not increase the likelihood of exacerbation of Hodgkin's disease, termination of pregnancy does not seem to be justified as a routine measure. Pregnancy may, however, obscure or delay the diagnosis of an exacerbation of the disease, and may also prevent its correct treatment in that full doses of X-ray therapy or of a cytotoxic agent such as nitrogen mustard cannot be safely used in the presence of a growing foetus *in utero*. This particularly applies during the first 3 months of pregnancy.

Berkeley and Bonney (1913) and Browne (1951) recommend termination of pregnancy in Hodgkin's disease. It is considered, however, that this should be reserved for cases with an exacerbation demanding urgent and full dose therapy, and cases where the inguinal and abdominal glands are particularly affected and require treatment, i.e., where the foetus cannot possibly be shielded from the damaging effects of the X-ray therapy. Some of the 50 per cent of pregnant patients who inevitably relapse during pregnancy will be fortunate in that the relapse is delayed until the last 6 to 8 weeks of pregnancy. They can then have both a live (if premature) child by termination of the pregnancy, and the optimum therapy soon after.

The first personal case was delivered about a year ago of her first and only child. The pregnancy was complicated as early as 20 weeks by a bout of so-called "pyelitis" which was treated with apparently good effect. The "pyelitis" recurred however at 28 weeks, and, even when the urine was sterilized and rendered pus-free with what appeared to be the correct antibiotic, the patient had persisting pyrexia and tachycardia; she looked ill and had a severe and resistant normochromic anaemia. She went into premature labour at 36 weeks and delivered herself spontaneously of a healthy 5 pounds infant. Thereafter the pyrexia (plus a disproportionate tachycardia) continued unabated, and did not respond to the gamut of modern antibiotics. One month postpartum, a small mass in the right flank and right epigastrium was found. Laparotomy was performed, and the liver was found to be grossly enlarged with multiple tumour nodules throughout. A biopsy was taken from one of the nodules in the left lobe of the liver. This showed some of the typical features of Hodgkin's disease, Dorothy Reed or Reed-Sternberg cells, infiltration with eosinophils and lymphocytes and intervening fibrosis.

This patient was subsequently treated with intravenous nitrogen mustard, the last treatment being in October last. She cannot be said to be well; her liver is considerably enlarged (although she has no lymphadenopathy), and she has a persistent secondary anaemia, anorexia and lassitude. Nevertheless, her life has been prolonged by the therapy, although her expectation of life is probably no longer than 2 years.

This patient's disease appeared to be mainly hepatic and intra-abdominal with, in addition, enlargement of the glands in the hila of both lungs and early infiltration of the right lung. She appears to have been among the relatively fortunate patients whose exacerbation was confined to the second half of her pregnancy, although the delay in making the diagnosis and in starting treatment may in the long run influence unfavourably the prognosis in her case.

The second personal case was also primigravid and in her thirties. Her history was of generalized pruritus of 4-years duration, enlarged neck glands of 7-months duration, and malaise, anorexia and loss of weight. During the month before attending as an out-patient, she had had a choking sensation, breathlessness on slight exertion, and an unproductive cough. The diagnosis of Hodgkin's disease was made by biopsy of a neck gland. She had considerable enlargement of the mediastinal lymph glands, but as there was no evidence of compression or obstructive symptoms, no treatment was instituted.

Five months later, however, she was admitted to hospital with mediastinal obstructive signs and symptoms and evidence of bilateral infiltration of the lungs. Her enlarged neck glands were now painful. She was then found to be 2-months pregnant. Advice was sought on the question of termination of the pregnancy. This was not performed because (1) the patient and her husband were extremely keen to have a baby; she was a nurse and knew about her illness and its prognosis, (2) the prognosis (for both mother and child) was poor in any case, (3) it was decided that irradiation of the thorax and neck only might be all the therapy immediately indicated. Following this last treatment, the patient's general condition improved and the mediastinal and lung foci were greatly diminished in size but not the cervical glands.

Subsequently the patient's general condition deteriorated rapidly and she had to be readmitted when only 21-weeks pregnant. She was then markedly anaemic, had a raised blood pressure (170/100), albuminuria, and a raised blood urea (120 mg. per cent, subsequently rising to 360 mg. per cent). She had lost a lot of weight, had had a recent epistaxis, and had a small tender swelling on her scalp. She had haematuria and a further epistaxis some days after admission.

In view of the obviously acute exacerbation of the disease, she was transferred to the Maternity Hospital for abdominal hysterotomy. Before this was performed, there was much debate as to the cause of the hypertension, albuminuria and uraemia. At this point it might be mentioned that the patient gave a previous history of so-called "nephritis" when aged 10 years, and that a small left "hydronephrosis" had been found in a London hospital in 1953, during the investigation of vague lower abdominal pain.

The hysterotomy was performed early in November, 1955. Post-operatively the patient's deterioration continued and she finally became jaundiced and had repeated epistaxis. She died 6 weeks after termination of the pregnancy, never having been fit enough for the resumption of any form of therapy. Post-mortem examination showed extensive involvement of the liver, lymph nodes, bowel lymphatics, gall-bladder, adrenals, pancreas, both kidneys, peritoneum, the choroid plexus on one side and the ovaries. The spleen was not involved. Histologically the growth was found to be a Hodgkin's sarcoma or reticulo-sarcoma.

It is difficult to fit this patient into any sort of pattern. She died of a very malignant and rapidly metastasizing tumour. Hodgkin's disease, in contrast, appears almost to be an inflammatory process with its cellular infiltrates and intermittent fibrosis, and its acute and chronic phases. True metastases do not seem to occur, and the theory that it is multicentric in origin seems at least plausible. If it is, then its treatment by surgery, and even by the irradiation of selected areas, has doubtful theoretical justification. The ideal would seem to be a chemotherapeutic agent which could become rapidly disseminated throughout the lymphatic part of the reticulo-endothelial system.

The management of Hodgkin's disease in pregnancy depends not only on whether the disease becomes worse as a result of the pregnancy, but also on whether the pregnancy itself is affected by the disease. According to Myles (1955), many outmoded ideas must be discarded in this respect. Abortion is not commoner in Hodgkin's disease than normally, nor is prematurity or post-partum haemorrhage. Labour is, on the whole, not affected, although many pregnancies may have to be terminated by elective Caesarean section for non-obstetrical reasons.

If treatment is necessary in the presence of a continuing pregnancy, firstly in a pre-viable one, termination and full therapy are indicated; secondly, in later pregnancy with the disease outwith the abdominal and inguinal areas radiotherapy to the thorax and cervical regions may sufficiently arrest the progress of the disease to justify delaying termination of the pregnancy, at least until near term. On the other hand abdominal and inguinal lesions (with an exacerbation of the disease) even after the 28th week of pregnancy, make immediate termination and early therapy imperative. Although most authors on this subject seem to regard X-ray therapy as the treatment of choice in Hodgkin's disease in pregnancy, some form of chemotherapy seems, as least theoretically, preferable. The nitrogen mustards do not seem to have any advantages over X-ray therapy, but possibly the less toxic triethylene melamine will be better than either, especially if it can be shown not to cross the placental barrier.

In conclusion, it might be mentioned that another patient is attending the Antenatal Clinic at present—a primigravida aged 21 years who is now 26-weeks pregnant. She appears not to have had an exacerbation of the disease for more than a year, and seems very well.

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Ion-Exchange Resins in Pre-eclamptic Toxaemia of Pregnancy

By Dr. Andrew W. Laughland, Victoria Infirmary, Glasgow

The case histories of 4 patients who developed severe pre-eclamptic toxaemia and were treated with ion exchange resins are presented. The reason for using a cation exchange resin in the treatment of pre-eclampsia was that, by binding sodium to its large molecule and thus decreasing sodium absorption from the gut, the beneficial effects which may follow reduction of dietary salt would be improved. The reason for wanting to induce a negative sodium balance in pre-eclamptic toxaemia was based on the widely accepted belief that salt retention occurred and that the degree of retention was related to the severity of the toxaemia. Dieckmann and Pottinger (1956) recently reported the surprising finding that intra- and extracellular sodium concentration is less in pre-eclamptic toxaemia than in normal pregnancy. The mechanism whereby an induced negative sodium balance exerts a beneficial effect must therefore be considered as yet unexplained.

The preparation of ion exchange resin which was used was that marketed by Eli Lilly and Co. under the trade name Carbo-Resin. This is a mixture of resins which represents an attempt to overcome the dual disadvantage of an uncompensated cation exchange resin which would reduce the absorption of potassium as well as sodium and would tend to produce acidosis.

The pre-toxaemic histories of the 4 cases were as follows: the pregnancy in the first 3 cases had been apparently normal until the 30th week, and in the fourth case until the 33rd week. Thereafter the patients all developed severe pre-eclamptic toxaemia. In all cases the oedema, hypertension and albuminuria were well marked, and all but one complained of headache. Just before commencing resin therapy and after a control period of at least 4 days, there was no improvement following bed rest, phenobarbitone sedation and a diet which contained one gramme of sodium as NaCl.

Case 1. This 27-years-old virtual primigravida had toxaemic signs and symptoms for 10 days before she was admitted to hospital. In addition to well marked generalized oedema, her blood pressure was 165/105 mm. Hg and her urine contained 4 parts Esbach of albumen. Abdominal examination indicated that she was about 8 weeks from term. Shortly after admission she began to complain of frontal headaches. During the control period of 4 days, she appeared to be deteriorating and delivery by Caesarean section would have been clinically justifiable. Ion exchange therapy was then started, using 15 g. thrice daily, but after 4 days this dosage was doubled for 8 days, during which time 18 pounds of weight was lost. This was associated with a diuresis and a loss of oedema. A less dramatic but nevertheless satisfactory improvement in albuminuria and hypertension then occurred, and, on the day before her expected date of delivery, labour commenced 3 hours after surgical induction. The outcome was satisfactory, the labour lasting 4½ hours and a live male child weighing 5 pounds being spontaneously delivered. The placenta was small and was infarcted. The patient then had an uneventful puerperium, and when dismissed was normotensive and free from albuminuria. At follow-up 2 and 6 months after delivery, the patient was normotensive and examination of the urine revealed no abnormality.

In this case resin therapy brought about a rapid reduction of weight due to the mobilization of oedema fluid, the result of an induced negative sodium balance. Cation exchange resin therapy and a low salt diet has been estimated by Hutchinson and Plentl (1954) to give up to a 40 per cent reduction of body sodium. Previously it could have been postulated that the other beneficial effects which are demonstrated in this case were due to a reduction in retained sodium. This may still be true, but if the work of Dieckmann and Pottinger (1956) is accepted, we must assume that any beneficial effects of therapy in this case were due to the mobilization of the retained water *per se*.

Case 2. This patient was referred for admission to hospital by her own doctor, as a case of pre-eclampsia. During her two previous pregnancies antenatal care had been conducted by her own doctor and they were reported as normal, as was her present pregnancy up to the 32nd week. On admission, she gave a history of progressive generalized oedema for 10 days, with recurrent headaches for 3 days, and was found to have a blood pressure of 170/110 and 6 parts Esbach albuminuria. Abdominal examination showed that she was 32-weeks pregnant. During the control period of 4 days, she showed no evidence of improvement, and early termination of pregnancy would have been justifiable. Two days after ion exchange resin therapy was commenced, using 45 g. daily, a diuresis began and within 7 days she had lost 11 pounds. The improvement in the hypertension was, however, slight and after temporary arrest of toxaemic signs she began to deteriorate. Five days before her expected date of delivery she entered labour spontaneously, and after 26 hours was delivered of a live female child weighing 5½ pounds. The placenta was heavily infarcted. The progress in the puerperium was satisfactory in this case, and, on dismissal and at follow-up until 6 months after delivery, she was normotensive and free from albuminuria.

The blood pressure in this case was not influenced by the negative sodium balance and only after delivery did she lose her hypertension. The fact that she remained normotensive after delivery suggests that she was normotensive before the pregnancy began. According to Dieckmann and Pottinger (1956) however, this patient, a gravida-3, should be suspected of having latent hypertensive tendencies, and if this is accepted, it might be

postulated that the hypertension was not of an identical aetiology to the first case.

Case 3. This primigravida was admitted during the 35th week of her pregnancy, and stated that until the 30th week she had remained well. She then noted slight but persistent ankle oedema. During the 4 days prior to admission, she had rapidly developed well marked oedema, which was associated with occasional headaches and anorexia, and on admission she had a blood pressure of 150/100. After the 4-days control period, headache and anorexia were troublesome, her blood pressure was 150/95 and her urine contained 8 parts Esbach of albumen. Carbo-resin therapy was started and after 7 days she had lost 7 pounds and looked quite different, her blood pressure being within normal limits and the albuminuria less marked.

After a further week, when her blood pressure was 150/105, and when she was on the point of refusing to take any more Carbo-resin, labour was induced, and after a latent period of 20 hours and a 14-hour labour, the patient was spontaneously delivered of a live female child weighing 5 pounds 2 ounces. She was then 3 weeks from her expected date of delivery, and the placenta was normal in appearance. After delivery, the albuminuria soon cleared up, but, still hypertensive, the patient was allowed home. After 2 months the blood pressure was 135/50. This case resembles the first with everything speeded up, the weight loss was accompanied by a diuresis and a disappearance of oedema, and then after a 10-day period of improvement deterioration occurred. With more co-operation from this patient, further prolongation of the pregnancy would probably have been attempted.

Case 4. The last case was a primigravida who had remained well until the 33rd week of pregnancy. She had then developed persistent oedema and when this became well marked and associated with hypertension and albuminuria she was referred to hospital by her own doctor. After 4 days with no improvement ion exchange therapy was commenced and following a marked diuresis, 17 pounds of weight was lost in 7 days. The hypertension and albuminuria did not deteriorate, but did not improve, and, when 12 parts Esbach of albumen was reported to be present in her urine, artificial rupture of the membranes was performed.

Her general condition and appearance did not, however, suggest imminent eclampsia, as it had previously, and the rather long induction-delivery interval of 76 hours did not, therefore, encourage us to consider delivery by Caesarean section. The labour, which lasted 8 hours, ended in the spontaneous delivery of a live male child weighing 6¼ pounds, the patient being then 4 weeks from her expected date of confinement. In this case the placenta appeared to be normal. When this patient was dismissed 11 days after delivery, her blood pressure was 130/85, and she still had a trace of albuminuria. In this case the behaviour of the blood pressure during the year following delivery suggested that this patient's response to stress included the appearance of a hypertension, and she may thus be similar to the second case and different from the other two in that the hypertension was not affected by the negative sodium balance.

Discussion

While illustrating the beneficial effects which may follow the use of ion exchange resins, it is suggested that the hypertension may in part be due to an electrolytic upset which can be favourably influenced by inducing a negative sodium balance. All the patients who were given Carbo-resin therapy were first investigated in several ways, and one test which was applied to these cases was the observance of the effect on the hypertension of an intravenous injection of TEAB. In the present cases this ganglion blocking agent had no hypotensive effect which, according to Brust, Assali and Ferris (1948) signifies that in pre-eclampsia the high blood pressure is in part at least due to some factor which effectively blocks or counteracts the depressant effect of ganglion-blocking agents. An upset in the electrolytic balance within the body cells may be this factor, as ion exchange resin therapy can improve the hypertension and can make a hypertension due to toxaemia become sensitive to TEAB.

Carey (1953) states the case for relating the oedema, the hypotension and the tendency to convulsions to sodium retention, and he quotes Rosenheim (1951) who relates the control of the basal blood pressure, and Hodgkin and Katz (1949) who relate the initiation of nerve impulse, to the Na/K ratio within and without the cells concerned. If Carey (1953) is correct the effect of ion exchange resin is the depletion of body sodium. If, however, Dieckmann and Pottinger (1956) are correct, that is that intra- and extracellular concentration of sodium is reduced in toxaemias, the beneficial effects of ion exchange resin therapy must be differently explained. It may be postulated that, by reducing sodium intake, a diuresis is encouraged, but that, because the intra- and extracellular concentration of sodium is already low, a degree of tubular reabsorption of sodium is achieved, that, when related to the reduced extracellular and intracellular water content, partially or totally corrects the abnormal sodium concentration and Na/K ratio. The immediate interest in ion exchange resin therapy in pre-eclampsia is not, however, in such theorizing but rather its place in the treatment of the toxaemic patient, especially one where the disease becomes severe at a stage of pregnancy where termination involves the risk of prematurity.

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HOSPITAL REPORTS

BY

J. S. TOMKINSON, M.B., F.R.C.S., M.R.C.O.G.,

CLINICAL REPORTS FOR 1954 OF THE MATERNITY HOSPITALS OF THE TEACHING HOSPITALS BOARD OF THE UNIVERSITY OF CAPE TOWN

(1) THE PENINSULA MATERNITY HOSPITAL; (2) THE GROOTE SCHUUR HOSPITAL, WARD C.10; (3) THE MOWBRAY MATERNITY HOSPITAL; (4) THE NEW SOMERSET HOSPITAL, SHIPLEY WARD; (5) THE ST. MONICA'S MATERNITY HOSPITAL

THESE hospitals have prepared separate reports. It is stated that they work as one functioning unit; as there is selection of cases (for instance, medical disorders of pregnancy are referred to the Groote Schuur Hospital as far as possible) it would not be advantageous to compare the results of the separate hospitals. Different standards are used, as in the case of puerperal pyrexia, so it is sometimes difficult to make any real comparison.

The Foreword mentions "Up to the present there has been no relief in the obstetrical bed situation of the Cape Peninsula. The nursing and medical staffs work under great difficulties but yet manage to set a high standard. The 'turn-over' therefore remains appalling and the admission of non-booked cases stays at a dangerously high level. The situation has become a matter of extreme urgency." Patients are often transferred home on their 2nd and 3rd day after delivery, attended by midwives of the institution or by district nurses.

A Flying Squad is based on the Peninsula Maternity Hospital and is being used with increasing frequency.

All patients attending the antenatal clinics have a routine chest X-ray film taken. "A surprisingly low number of positive tuberculous lesions have been detected. The brunt of the work in connexion with pulmonary tuberculosis in pregnancy falls upon the Shipley ward in the Somerset Hospital."

The reports follow the recommendations of the Royal College, usually with a preamble to the separate tables. The total number of patients delivered in the 5 hospitals was 6,601, with 1,112 delivered on the district; 2,914 attended for a postnatal examination. Nineteen maternal deaths occurred, 7 of them at the Groote Schuur Hospital out of a total of 562 patients delivered, this being the hospital taking the medically complicated cases. Of these 19 deaths, 7 were from eclampsia (2 had a rupture of a haematoma of the liver into the peritoneal cavity) and 5 were associated with a post-partum haemorrhage. Fifty-four cases of eclampsia were seen, 39 in unbooked cases.

There was a well-marked difference in the incidence of syphilis between the hospitals, 466 patients attending at the New Somerset Hospital (1,709 deliveries) and only 15 at the Mowbray (1,027 deliveries), probably due to differences in status.

One hundred and thirty-two twin deliveries occurred, an incidence of about 1 in 50, and 5 triplet deliveries, an incidence of 1 in 1,500. Breech deliveries totalled 286, with an uncorrected perinatal mortality of 32 per cent. Contracted pelvis occurred 134 times, Caesarean section being performed in 117 cases. A post-partum haemorrhage occurred 615 times; the technique of managing the third stage appears to vary from hospital to hospital, indicated in the differing incidence in manual removal of the placenta. Out of a total of 618 Caesarean sections, 20 were of the classical type. The incidence of forceps delivery varied from the highest of 7·8 per cent to the lowest of 2·9 per cent.

The stillbirth rate differed between the extremes of 7·2 and 1·4 per cent; the neonatal death rate was between 7·2 and 1·9 per cent. There was a high incidence of premature liveborn infants at the Groote Schuur Hospital (24·5 per cent) and of these 20 per cent died neonatally; the lowest incidence of premature liveborn infants was 6·4 per cent, with a neonatal loss of 10·6 per cent.

These reports, taken collectively, indicate that there is a great deal of interesting material available for the teaching and investigation of obstetrics in the University of Cape Town. The conditions may not be ideal from the public health aspect yet there is first-class experience to be gained by clinicians and students.

THE ANNUAL REPORT OF THE DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY OF THE UNIVERSITY OF OTAGO, NEW ZEALAND, 1954

THE obstetric work has been performed in the 45 antenatal and postnatal beds (with 5 beds for patients in waiting) of the Queen Mary Maternity Hospital, with a premature baby unit of 6 cots. The patients are local bookings and emergency cases from the district up to 100 miles around Dunedin.

There were 819 babies born from 808 deliveries, of which 183 were unbooked cases. No maternal deaths occurred. At the postnatal clinic 533 patients attended. An episiotomy was performed in 170 cases and there were 2 cases of a third degree tear of the perineum. Labour was induced medically 67 times and surgically 40 times; only 3 cases failed out of the total of 107, all of them being delivered by Caesarean section. The inductions were most commonly done for toxaemia or

postmaturity. There was a 6 per cent incidence of pre-eclampsia, essential hypertension and chronic nephritis. One case of acute nephritis diagnosed at the 8th week was in hospital throughout the pregnancy, had a maximum of 16 grammes per litre of albumin and had a spontaneous delivery at term of an infant weighing 5 pounds 9 ounces. Four cases of eclampsia occurred, 3 in unbooked patients; all were delivered successfully. The 6 cases of placenta praevia were all treated by lower segment Caesarean section. Twenty-nine cases of uncomplicated and complicated breech delivery occurred, with a total foetal loss of 3 directly attributable to the delivery.

Primary post-partum haemorrhage occurred in 33 cases (4 per cent), of which 4 had the placenta removed manually. The Caesarean section rate was 5·8 per cent, all lower segment sections except 2 repeat classical operations. Only 6 cases of pyrexia due to genital tract infection were recorded, an incidence of 0·8 per cent. The forceps rate was 7·9 per cent.

Concerning the babies, 13 cases of haemolytic disease of the newborn occurred, of which 7 survived. All the patients appear to have been allowed to go into labour spontaneously. The corrected stillbirth and premature liveborn infant rates were 3·4 and 2·0 per cent respectively.

SIR WILLIAM GILLIATT MEMORIAL FUND

UNDER distinguished patronage a fund has been opened to raise a memorial to Sir William Gilliatt. The Fund will be held in trust and be administered by the Royal College of Obstetricians and Gynaecologists and it will be devoted to the aims of this College with which Sir William Gilliatt was so long associated and of which he was for three years President.

In a letter announcing the establishment of the Fund, which appeared in *The Times* on 26th October, it was stated that over £9,000 had already been received.

Donations should be sent to the Sir William Gilliatt Memorial Fund, Royal College of Obstetricians and Gynaecologists, 58 Queen Anne Street, London, W.1.

XVII[e] CONGRÈS D'OBSTÉTRIQUE ET DE GYNÉCOLOGIE DE LA FÉDÉRATION DES SOCIÉTÉS DE LANGUE FRANÇAISE

THIS Congress will be held in Marseilles from 9th to 12th September, 1957.

The Secretary-General of the Congress is Professor H. Serment, Hôpital de la Conception, Marseilles, to whom enquiries should be addressed.

SEVENTH INTERNATIONAL CANCER CONGRESS

THIS Congress, sponsored by The International Union Against Cancer, will be held in London from 6th to 12th July, 1958. The Congress headquarters will be the Royal Festival Hall.

There will be two main Sessions: (*a*) Experimental and (*b*) Clinical and Cancer Control. Special emphasis will be placed on Hormones and Cancer, Chemotherapy, Carcinogenesis and Cancer of the Lung.

Proferred papers will only be considered if submitted with an accompanying abstract (not over 200 words) before October, 1957, and if dealing with new and unpublished work.

Registration forms and a preliminary programme will be available early in 1957 on application to The Secretary-General, 45 Lincoln's Inn Fields, London, W.C.2.

BOOK REVIEWS

"A Textbook of Gynaecology." By JAMES YOUNG, *D.S.O.*, M.D., F.R.C.O.G., F.R.C.S.E., Emeritus Professor of Obstetrics and Gynaecology, University of London. Tenth edition, revised, in collaboration with J. C. MCCLURE BROWNE, F.R.C.O.G., F.R.C.S.E., Professor of Obstetrics and Gynaecology, University of London. Pp. xi+523, with 297 illus. A. & C. Black, London, 1956. Price 45*s*.

JAMES YOUNG, whose textbook of gynaecology has served successive generations of students for 35 years, has revised the latest edition in collaboration with Professor McClure Browne. If one were restricted to a single adjective to describe this book, it would be "solid", with the chapter on pain in gynaecology and backache a model of sound writing. Yet in a work avowedly intended primarily for students and practitioners, and not for specialists, more emphasis might be laid on "medical" and less on "surgical" gynaecology. The authors indeed write that they believe that much of the time undergraduates spend in the operating theatre is wasted. Appropriately, therefore, the next edition might devote more space to conditions such as trichomonas vaginitis and pruritus vulvae, and more stress might be laid on the psychosomatic basis of many gynaecological symptoms and syndromes. The general practitioner would also appreciate a critical chapter on hormone therapy in gynaecology, while the student would be grateful for a section on sexual problems including frigidity and contraception, as he finds them not considered in his other textbooks. All these are subjects on which the family doctor's advice is commonly sought.

The inclusion of a chapter on abortion also merits consideration, for it enters into the differential diagnosis of many gynaecological symptoms. All this would necessitate enlargement of the book, but the senior author has never hesitated to find room for new subject-matter. Indeed this new edition includes two new chapters—on bilharziasis of the female genital tract and on syphilis, granuloma inguinale and lymphopathia venereum; while the chapters on genital tuberculosis and on inflammations of the vulva and vagina have been completely re-written.

"The Premarital Consultation, a Manual for Physicians." By ABRAHAM STONE, M.D., and LENA LEVINE, M.D. Pp. 90, with 11 figs. Grune and Stratton, Inc., New York and London, 1956. Price 3 dollars.

A PREMARITAL consultation is not so commonly sought in this country as in the U.S.A., although the National Marriage Guidance Council and similar bodies are trying to popularize it here. Perhaps this is partly because most medical students receive little or no instruction on the subject, and many family doctors are embarrassed rather than pleased when their advice is sought in this context. Dr. Stone and Dr. Levine, both well-known in the sphere of marriage guidance, have written a useful little book for doctors, in which they describe how to advise on the social, economic, emotional, sexual and genetic aspects of marriage and family life. They answer, partly in verbatim interview style, the questions engaged couples ask, and, more important, they tell the doctor how to elicit the questions the couples hesitate to ask. This small book contains a large amount of wisdom.

"Obstetric Practice." By H. SPEERT, M.D., Associate in Obstetrics and Gynecology, Columbia University, New York, and A. F. GUTTMACHER, M.D., Clinical Professor of Obstetrics and Gynecology, Columbia University and Director of Department of Obstetrics and Gynecology, Mount Sinai Hospital, New York. Pp. 478. McGraw-Hill, London, 1956. Price 52*s*. 6*d*.

THIS is an excellent book with many virtues to commend it—a clear and concise text, facile and even elegant writing, a human approach, a handy size, clear print and reasonable price. Surprisingly, the absence of illustrations appears no drawback. One of a "Handbooks for the General Practitioner" series, it clearly demonstrates that those who follow its teachings will offer their patients a high standard of obstetric care. But the reader in this country will note that it is implied that the general practitioner has beds in a fully-equipped hospital at his disposal. He may also consider that much of the operative obstetrics described is outside the scope of the general practitioner-obstetrician; but this may be because the indications for consultations with a specialist are not clearly given.

There are few controversial statements, but restitution and external rotation are described as if synonymous; similarly lie and presentation, and constriction and pathological retraction rings. A most useful feature is a table of the chances of the repetition of various congenital abnormalities in successive babies in the same woman. And it is interesting to learn that Anne Boleyn may have been beheaded because she showed the sign of a witch—an axillary breast.

REVIEW OF CURRENT LITERATURE

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PHYSIOLOGY

391. **Histochemical Observations on the Endometrium. I. Normal Endometrium.**

By D. G. McKay, A. T. Hertig, W. A. Bardawil and J. T. Velardo. *Obstet. Gynec.*, **8**, 22–39. July, 1956. 37 figs. 1 col. plate. 24 refs.

This is a report on certain histochemical observations on normal human endometrium in 60 cases of hysterectomy. Estimations were carried out for ribonucleoprotein, alkaline and acid phosphatases, specific esterase, 5-nucleotidase, glycogen, glycoprotein and inorganic iron. Of the 60 specimens, 15 were proliferative, 39 were progestational, and 6 were associated with early pregnancy.

Most of the biochemical alterations were due to changes in the glandular and surface epithelium, whereas the stroma and blood vessels contributed only slightly. Ribonucleoprotein, which is known to be associated with protein synthesis, is present in increasing amounts reaching a peak in the late proliferative phase and decreasing in the progestational phase. The same applies to alkaline phosphatase activity. Acid phosphatase is low in the proliferative phase and increases in the secretory phase, as is glycogen.

J. G. Dumoulin

PREGNANCY

392. **Changes in the Symphysis Pubis in Pregnancy and the Puerperium.** (Su particolari alterazioni della sinfisi pubica in gravidanza ed in puerperio.)

By L. Bellomi and R. D'Alo. *Ann. Ostet. Ginec.*, **77**, 987. Nov. 1955. 9 figs. 28 refs.

During pregnancy, there is a gradual widening of the symphysis pubis. This has been measured by various authorities and the mean increase varies from 4·2 mm. in primigravidae to 5·4 mm. in multigravidae. In young women, whether primigravidae or multigravidae, the mean increase is greater, namely 6·7 mm. This change contributes significantly to the widening of pelvic capacity which is evident at the end of pregnancy.

Certain bony changes may become apparent in the pubic bones; these include rarefaction of the margins of the bones, irregularities in the articular surfaces and pseudo-cystic areas of rarefaction. During the puerperium, the condition returns to normal with recalcification.

Rupture of the symphysis may occur during difficult labour or instrumental delivery. This may be followed by an osteitis of the pubis, similar to that encountered following retropubic operations such as prostatectomy.

Josephine Barnes

393. **The Cardio-Thoracic Ratio in Roentgenography of the Normal Pregnant Patient.**

By M. ROLLINS and F. J. BONTE. *Amer. J. Roentgenol.*, **76**, 64–69. July, 1956. 2 figs. 10 refs.

A postero-anterior roentgenogram of the chest made at a distance of 6 feet gave a fairly accurate representation of the intra-thoracic structures with an error of less than 5 per cent. Utilizing measurements of the transverse diameter of the heart and the greatest internal width of the chest, a cardio-thoracic index was worked out which showed that the heart occupied about 45 per cent of the total transverse measurement. In pregnancy, both diameters tend to increase slightly, the ratio remaining more or less unchanged; but the authors decided that a ratio of more than 55 per cent should be regarded as abnormal.

John H. Mulvany

394. **Radiology in Obstetrics.**

By C.-E. JOHANSON. *Acta obstet. gynec. scand.*, **35**, 181–270. 1956. 48 figs. 127 refs.

Hysterosalpingography.

By V. MADSEN. *Acta obstet. gynec. scand.*, **35**, 271–329. 1956. 22 figs. 51 refs.

These two papers, the former from Helsingfors (Finland), the latter from Copenhagen (Denmark), represent opening lectures to be given before the Ninth Congress of the Northern Association of Obstetricians and Gynaecologists which will be held in Oslo in August, 1956. The papers are critical evaluations of radiological methods in obstetrics and gynaecology and are worth reading in the original because of the conciseness and clarity of the presentation and because of the beauty of the plates and line drawings.

N. Alders

395. **Body Composition and Body Water Metabolism in Normal Pregnancy.**

By H. B. HALEY and J. W. WOODBURY. *Surg. Gynec. Obstet.*, **103**, 227–232. Aug. 1956. 5 figs. 15 refs.

Established techniques for the study of water metabolism using deuterium oxide (D_2O) have been employed in Boston, Massachusetts to study certain phases of water metabolism during normal pregnancy. Total body water was determined at 4 to 6 week intervals during the last 2 trimesters of pregnancy and during the puerperium in 3 normal subjects. All showed a similar gain in body weight, total body water and body solids, with the water as a fraction of the body weight remaining relatively constant during most of the pregnancy. During the last 2–4 weeks there was an increase in body water equal to or greater than the weight gain, with body solids remaining quite constant.

Serial determinations of pre-partum water turnover rates were made but none showed significant change and all were within the normal non-pregnant range.

The determination of equilibrium times after injection and the simultaneous D_2O analysis in maternal serum, cord blood serum, placental tissue water, colostrum and milk indicate that all water in the mother, in the foetus and in the other products of conception is in distributional equilibrium and that this equilibrium is established at rates similar to those in the non-pregnant subject.

Determinations of body weight, water and solids made after delivery, revealed that in the first 7 days there are profound changes in water metabolism evidenced by an elevated water turnover rate abruptly falling to normal. In the same week there is a nearly constant loss of body solids with a wide range of changes in total body water.

John P. Erskine

396. **Adrenal Steroids in Human Placenta.** (Bijnierschorssteroiden in menselijke placenta.)

By J. L. MASTBOOM, A. M. COHEN and M. VAN GARDEREN. *Nederl. Tijdschr. Verlosk. Gynaek.*, **56**, 362–363. 1956.

Fresh placentae were minced and extracted with ethyl acetate. The extract was fractionated chemically, removing some unwanted lipids, and then further analyzed by paper chromatography. By development with triphenyltetrazolium chloride a spot was found showing the same Rf value as cortisone. This material was further characterized by determining its absorption spectrum in sulphuric acid. Although the identification of the compound is insecure and no quantitative data are given, it is likely that the authors' claim that cortisone occurs in the placenta is true. This work provides an incentive for the firm identification of cortisone from the placenta and suggests a reason for the well-known fact that Addison's disease may show a remission in pregnancy.

Arnold Klopper

397. **Hypertension Associated with Pregnancy.**

By J. H. CURRENS, D. E. REID and J. L. NEWELL. *J. Amer. med. Ass.*, **161**, 1232–1239. July 28, 1956. 4 figs. 14 refs.

The first part of this study from the Boston Lying-In Hospital compares the recent incidence of hypertension associated with pregnancy with the incidence in a period 10 years before. From 1941 to 1944 the incidence was 87 per 1,000, and from 1951 to 1954 the comparable figure was 47 per 1,000. The analysis shows a striking decrease in the number of cases of pre-eclampsia and general improvement in prenatal care, and limitation of sodium intake is considered to be the reason for this.

The authors then discuss the treatment of hypertension in pregnancy with proveratrine. The usual classification of the toxaemias is used and details of 21 cases are given. Eight of these cases were classified as pre-eclampsia, nine as hypertensive vascular disease, and four as hypertensive disease with added pre-eclampsia. Proveratrine was given orally or intravenously according to the rapidity of action required. The oral dose in general ranged from 0·5 to 1·5 mg. every six or eight hours but the method of trial and error is necessary to arrive at a suitable dose. For intravenous use 0·12 mg. was given, sometimes in the form of a slow infusion. Proveratrine is considered to be an improvement of the time-honoured use of Veratrum in the treatment of toxaemia of pregnancy and to have certain advantages over the use of other hypotensive drugs.

D. W. James

398. **Diagnosis of Antepartum Shock.** (Zur Diagnostik des antepartalen Schocks.)

By H. WINZELER. *Gynaecologia, Basel*, **141**, 247. Apr. 1956.

One case of ante-partum shock is described. This condition has not been recorded in European literature, although recognized by Americans who describe it as the supine hypotensive syndrome.

American experimental workers, Menger, Goodson *et al.*, have created shock by ligating the inferior vena cava in dogs. The same occurred in 2 women when the inferior vena cava was compressed digitally after laparotomy for Caesarean section prior to incising the uterus. These workers conclude that the supine hypotensive syndrome is due to mechanical compression by the gravid uterus of the inferior vena cava, so preventing the blood flow to the heart. This syndrome, according to American workers, occurs in approximately 11 per cent of pregnant women when lying supine or in a slight Trendelenburg position, but the shock is immediately relieved by assuming the lateral position. If, however, the hypotensive shock lasts too long, abruptio placenta may occur.

The author stresses the danger of the supine position during pregnancy if the patient shows any sign of shock. Failure to appreciate this syndrome caused the author to perform an unnecessary Caesarean section.

[This seems an important syndrome to bear in mind, and may explain some cases of abruptio placenta.]

Jean L. Hallum

399. **Aldosterone Excretion in Normal and Toxaemic Pregnancies.**

By J. D. MARTIN and I. H. MILLS. *Brit. med. J.*, **2**, 571–573. Sept. 8, 1956. 38 refs.

The authors, from St. Thomas's Hospital, London, have investigated the urinary excretion of aldosterone in normal pregnancy and in toxaemic patients. The method used was a physico-chemical one—a slight modification of that of Neher and Wettstein. By this method, after the addition of 6 μg. of pure aldosterone to urine, there was a recovery of 55 per cent on the final chromatogram.

Urine was collected from 55 normal pregnant women, and from 20 with toxaemia of late pregnancy. The criteria of toxaemia were the development after the 28th week of a blood pressure of 140/90 or more, with albuminuria and oedema. The values at various stages of pregnancy were charted. The normal range in men and non-pregnant women was up to 2 μg. per day, with a mean and S.D. of $0{\cdot}6 \pm 0{\cdot}5$. During pregnancy the values tended to increase and went up to 10 μg. per day. In toxaemia the amounts excreted were within the range for normal pregnancy. The authors discuss their findings, and suggest that the increased aldosterone secretion in normal pregnancy may be to counteract the sodium excreting effects of progesterone.

Eileen Wilson

400. **Effective Uterine Blood-Flow During Exercise in Normal and Pre-eclamptic Pregnancies.**

By N. MORRIS, S. B. OSBORN, H. P. WRIGHT and A. HART. *Lancet*, **2**, 481–484. Sept. 8, 1956. 4 figs. 9 refs.

Since in many cases of pre-eclampsia, rest in bed may alone bring about a fall in blood pressure to within normal limits, whereas deterioration often follows the continuation of a normal life, the authors considered it of interest to discover whether exercise altered the effective uterine blood-flow. Observations were made in the uterine and quadriceps muscle blood-flow before, during and immediately after exercise in 21 normal and 19 pre-eclamptic women. A measure of the blood-flow was obtained from the rate of removal of a diffusable ion (^{24}Na). A rise of systolic and diastolic blood-pressure occurred with exercise in both normal and pre-eclamptic patients, and with these changes there were alterations in the blood flows of both uterine and quadriceps muscles. During exercise there was an increase in leg-muscle blood-flow and at the same time a reduction in the uterine blood-flow. In normotensive women the uterine flow during exercise often approached that recorded in pre-eclamptic patients at rest. In the pre-eclamptic women the uterine blood-flow which was already reduced while resting decreased still further during exercise. On cessation of the exercise the changes in leg and uterine blood-flow were reversed. Both at rest and during exercise the effective uterine blood-flow was found to be inversely correlated with the diastolic blood-pressure, the greater the diastolic blood-pressure the less is the effective uterine blood-flow. Though the pressor mechanism in pre-eclampsia has not yet been elucidated the authors believe that as the intensity of the vasospasm increases it will progressively reduce the blood-flow in the splanchnic organs. In the extreme case the additive effect of reduction of uterine blood-flow by exercise and that dependent on the pre-eclamptic vasoconstriction might endanger the growth or viability of the foetus.

H. H. Fouracre Barns

401. **Reversible Glomerular Lesions in Toxaemia of Pregnancy.**

By V. E. POLLAK, C. L. PIRANI, R. M. KARK, R. C. MUEHRCKE, V. C. FREDA and J. B. NETTLES. *Lancet*, **2**, 59–62. July 14, 1956. 5 figs. 8 refs.

The authors record the results of needle biopsy of the kidney in ten patients with toxaemia of late pregnancy. The biopsies were taken in the later weeks of pregnancy and again after delivery. On the basis of histological findings the patients were divided into three groups. The first group consisted of cases with swelling of the glomerular tufts; the second group, cases with swelling of the glomerular tufts, thickening of the basement membrane and some mild arteriolar sclerosis; and the third group of cases with predominant vascular sclerosis. The authors conclude that two distinct lesions were found in the women with toxaemia of pregnancy. Either generalized swelling of glomerular tuft or thickening of the basement membrane associated with vascular

changes were seen. These lesions are the probable pathological counterpart, respectively, of pre-eclampsia and essential hypertension with nephrosclerosis.

H. H. Fouracre Barns

402. **Pyelonephritis Masquerading as Toxemia of Pregnancy.**

By F. A. FINNERTY, Jr. *J. Amer. med. Ass.*, **161**, 210–214. May 19, 1956. 13 refs.

A toxaemia clinic was formed at the District of Columbia General Hospital three years ago and from the first 1,130 patients examined the author has separated 73 cases which were finally proved to have pyelonephritis. Most of the cases were young primigravidae referred because of albuminuria.

The three manifestations of pyelonephritis as shown by urinalysis are: (1) Clumps of white blood cells in the urinary sediment, (2) Pyelonephritis cells (glitter cells). These are large, pale, blue-staining cells with a tendency to variation in size and shape, to vacuolation, and Brownian movement of their cytoplasmic granules, and (3) positive urine culture.

To make the diagnosis at least two of the above manifestations should be present. Of the 73 cases 37 were ante-partum and 36 were post-partum. Sixteen of the ante-partum and 10 of the post-partum cases were finally diagnosed as pure pyelonephritis. In the remainder the diagnosis was pyelonephritis plus some other form of toxaemia or hypertension. Pyelonephritis during pregnancy is often asymptomatic and the importance of routine microscopic urinanalysis is emphasized. Therapy with either sulphonamides or antibiotics caused an improvement in all the patients in this series. The investigation did not demonstrate any relationship between pyelonephritis and toxaemia of pregnancy, but it clearly showed that the former often masquerades as the latter.

D. W. James

403. **Renal Function: Physiologic Basis for the Treatment of Pre-eclampsia-Eclampsia.**

By R. R. DE ALVAREZ. *Obstet. Gynec.*, **8**, 10–17. July 1956. 2 figs.

In the normal non-pregnant individual the glomerular filtration rate of the kidneys approximates to 125 ml. per minute which amounts to 180 litres per day. During normal pregnancy, a gradual increase in filtration occurs. By the ninth month the rate has increased from 50 to 75 per cent above the normal non-pregnant level but returns to pre-pregnant levels at term. In patients with pre-eclampsia or eclampsia a marked reduction in the glomerular filtration rate occurs, often to levels of 60 ml. per minute or even lower, probably due to vasoconstriction. In severe cases, the vasoconstriciion causes nephron damage which is evident by proteinuria. The blood supply to the tubules is also impaired so that they also are damaged with the result that reabsorption through them is greater. As a result, not only do oedema and hyperkalaemia occur, but also azotaemia.

Treatment of toxaemia should therefore include confinement to bed which permits no fluctuation of urine excretion. The diet should be low in sodium and high in protein. Neither dehydration nor over-hydration should be used: the fluid intake should be based on the anticipated total output—that is, the urinary output of the previous day plus 1,200 ml. The patient with toxaemia may suffer from electrolyte excess, particularly as regards the sodium ion, but treatment may, if not watched, produce a depletion of some electrolytes. There is no evidence that phenobarbitone affects renal function and it is therefore the sedative of choice. The combination of hydralazine and Rauwolfia in the severely ill patient improves renal function as well as lowering the blood pressure. Of the diuretics, ammonium chloride, when properly used, is very effective. Dextran is useful in anuric patients requiring maintenance of blood pressure. Digitalis is utilized in those with heart failure. Oxygen should be given in cases of cyanosis, dyspnoea and tachycardia.

The author states that most maternal deaths due to this condition result from fluid and electrolyte imbalance.

J. G. Dumoulin

404. **Clinical Experience with Bonadoxin in Hyperemesis Gravidarum.**

By C. R. CRAWLEY. *West. J. Surg. Obstet. Gynec.*, **64**, 463–465. Aug. 1956. 12 refs.

Bonadoxin is a mixture of 25 mg. meclizine dihydrochloride and 50 mg. pyridoxine hydrochloride (vitamin B_6). One tablet was given morning and evening to 65 patients with distressing nausea and vomiting in the first half of pregnancy. Twelve women (18 per cent) obtained excellent relief (relief within 24 hours) 41 (63 per cent) reported relief within a week of starting treatment; 8 had a fair result and 4 obtained no relief. The author concludes that the preparation is an effective agent in this condition.

D. C. A. Bevis

405. **Transfer of Radiosodium to Human Foetus in Late Pregnancy.**

By C. G. CLAYTON, F. T. FARMER and T. JOHNSON. *Lancet*, **2**, 539–543. Sept. 15, 1956. 9 figs. 11 refs.

The authors record their experiences in the investigation of placental efficiency by measuring the rate of accumulation within the foetus of a tracer dose of radiosodium injected intravenously into the mother. The measurement is made with a collimated scintillation-counter placed over the centre of the anterior aspect of the uterus. The method yields evidence of the more insidious types of placental ischaemia and has proved completely reliable as a means of diagnosing foetal death.

H. H. Fouracre Barns

406. **Transplacental Transmission of Foetal Erythrocytes with Demonstration of Foetal Haemoglobin in Maternal Circulation.**

By Y. M. BROMBERG, M. SALTZBERGER and A. ABRAHAMOV. *Obstet. Gynec.*, **7**, 672–674. June 1956. 11 refs.

Isoimmunization of an Rh-negative pregnant woman is presumably caused by transfer of foetal antigen across the placenta into the maternal blood. The authors (from Jerusalem, Israel) studied the amount of foetal haemoglobin in 72 women in the last trimester of pregnancy by the method of Singer and Chernoff based on resistance to alkali denaturation. The results ranged from 0 to 2·2 per cent of total haemoglobin with a mean of 1·45 per cent. In only 4 women was more than 2 per cent found indicating the presence of significant amounts of foetal haemoglobin. However, in 2 other pregnant women highly significant concentrations were found. The first was an Rh-negative isoimmunized patient who delivered an erythroblastotic infant. The second woman delivered a macerated stillborn foetus: she had hypertensive vascular disease complicated by toxaemia of pregnancy.

J. G. Dumoulin

407. **Foetal Death in Utero with Hypofibrinogenaemia.**
By R. F. JENNISON and A. H. C. WALKER. *Lancet*, **2**, 607–609. Sept. 22, 1956. 2 figs. 9 refs.

A case of hypofibrinogenaemia associated with intrauterine foetal death is reported. The authors point out that failure of blood coagulation most commonly occurs with premature separation of the placenta, eclampsia, retention of dead foetus or placental fragments, or embolism of amniotic fluid. Spontaneous bruising was the first symptom of the hypofibrinogenaemia and occurred when the foetus had been dead for some 8 weeks. The fibrinogen blood level was found to be low and remained so until after delivery when it rose spontaneously to normal without any administration of fibrinogen or blood. A test dose of fibrinogen (2 g.) was given ante-partum. This caused a temporary elevation of the fibrinogen blood level in the first 100 minutes, after which the blood content fell to its previous level within 24 hours. The authors suggest that this indicates the persistence of an active process capable of removing at least 2 g. of fibrinogen from the circulation within 24 hours.

H. H. Fouracre Barns

408. **Rhesus Immunization in Pregnancy.**
By H. M. PRETORIUS. *S. Afr. med. J.*, **30**, 739–743. Aug. 4, 1956. 14 refs.

An analysis of 66 cases of rhesus immunization seen at Addington Hospital, Durban, during a 2-year period (August, 1951–July, 1953) is presented. This represents an incidence of 1·62 per cent.

Two cases terminated in abortion and there were 10 rhesus negative babies. Of the 54 rhesus positive babies 47 had positive Coombs' tests and were clinically affected, whereas 6 with positive Coombs' tests were unaffected clinically. In 1 case the Coombs' test was negative.

Five babies were stillborn and there were 5 neonatal deaths. The causes of death were hydrops foetalis (3), macerated foetus (2), kernicterus (2), icterus gravis (2) and unknown (1).

It seemed that there was a natural tendency for rhesus positive babies to be delivered before the expected date. Of 15 cases with a "previous history" only 10 lived, whereas of 36 cases with no "previous history" 31 lived. Agglutinin titres did not prove very helpful from a prognostic point of view. Antenatal elicitation of pitting oedema of the foetal scalp is a valuable sign of hydrops foetalis.

The affected infant's condition at birth is placed into one of 3 categories, namely, severely, moderately or mildly affected. The presence of jaundice at birth or after a few hours is the most reliable sign of severity, and anaemia in the cord blood is the most valuable laboratory index. A pronounced megaloblast count is also highly suggestive, as is a raised serum-bilirubin level. Of the 53 Coombs-test positive infants 2 (3·8 per cent) developed kernicterus.

With regard to the management of these cases, vaginal delivery at term is favoured. There is no indication for premature induction nor Caesarean section.

Exchange transfusion is performed in severe and moderately severe cases, and the mild cases are observed and transfused if necessary. The technique of exchange transfusion is described. Blood from female donors was not found to be superior. Treatment of erythroblastosis foetalis by transfusion with sedimented red cells, as described by Pennell, is discussed. Breast feeding is allowed once the baby's condition is satisfactory.

Not a single case of Rh-immunization was seen in 784 Indian antenatal patients.

L. J. Abramowitz

409. **Prolonged Pregnancy.**
By A. STRAND. *Acta obstet. gynec. scand.*, **35**, 76–135. 1956. 29 figs. 145 refs.

This paper was given before the Ninth Congress of the Northern Association of Obstetricians and Gynaecologists at Oslo in August, 1956, and is a report on work undertaken at the Oslo Municipal Maternity Hospital and the Department of Obstetrics and Gynaecology of Oslo Rikshospitalet.

The author defines "prolonged pregnancy" as a pregnancy with an unusually long deviation in time beyond the mean duration of pregnancy, irrespective of the degree of development of the foetus, and fixes the limit of prolonged pregnancy at 294 days after the first day of the last menstrual period.

The material studied falls into two groups. One group deals with cases observed between 1918 and 1929, during which time no consideration was given to prolonged pregnancy, and this "untouched material" constitutes a control. The second group relates to the years 1947 to 1955 during which prolonged pregnancy was taken into account both for diagnostic and therapeutic purposes. The first group comprises 3,288 primigravidae and 2,622 multiparae, the second group consists of 2,092 primigravidae and 2,149 multiparae.

No correlation was found between maternal age and duration of pregnancy, though primigravidae of 35 years and over seemed to have a greater tendency to prolonged pregnancy than other age groups.

The perinatal mortality rate showed a clear tendency to rise with the duration of pregnancy after 280 days, particularly in primigravidae. The causes of this in-

creasing perinatal mortality rate were (*i*) a higher incidence of large infants, (*ii*) an increase in the duration of labour beyond that due to the increased foetal size, and (*iii*) a rising tendency to foetal hypoxaemia, increasing with the duration of pregnancy, due to changes in the physiology of the placenta.

There was a considerably higher incidence in prolonged pregnancy of signs of hypermaturity (lack of vernix caseosa resulting in maceration of the skin, particularly on the scrotum, labia majora, soles of the feet, palms of the hands; reduction in the amount of amniotic fluid; dehydration of the foetus resulting in disparity between length and weight; firm compression of the foetal body with marked kyphotic flexion of the spine and some overlap of the skull bones; as well as certain features of the centres of ossification on radiological examination).

Prophylactic (medicinal and/or surgical) induction of labour after critical evaluation of each individual case has reduced the perinatal mortality rate in the author's material.

Complications were not more frequent in induced than in spontaneous labours. Caesarean section was performed more often when the duration of pregnancy was longer than 294 days, particularly in elderly primigravidae and after failure of medicinal or surgical induction to produce uterine contractions.

[Compare abstract No. 410.]

N. Alders

410. **Prolonged Pregnancy.**

By A. LINDELL. *Acta obstet. gynec. scand.*, **35**, 136–163. 1956. 9 figs. 70 refs.

This paper was given before the Ninth Congress of the Northern Association of Obstetricians and Gynaecologists held at Oslo in August, 1956, and comes from a Stockholm and an Upsala (Sweden) Maternity Hospital. It is based on over 46,000 deliveries during the ten-year period 1943 to 1952. These are the author's main findings:

About 10 per cent of pregnancies have a duration of 294 days or more, and over 2 per cent continue for more than 300 days. This tendency to prolongation has no connexion with age or parity of the mother or the sex of the child.

Whilst the perinatal mortality at term is only 1·1 per cent, it increases progressively for each additional week of gestation; when delivery is delayed beyond 42 weeks the perinatal mortality approaches 4 per cent. This increase in mortality applies almost exclusively to the infants of primigravidae; in multiparae the perinatal death rate remains at about 1 per cent until the 44th week. The perinatal death rate increases with maternal age but no differences can be demonstrated between normal and prolonged pregnancies.

Birth-weight increases continuously with increasing duration of gestation until term is reached, but subsequent increase in weight takes place at a slower rate.

Most deaths among postmature infants occur during labour and the commonest cause of death is intracranial haemorrhage. The mortality in cases of induced labour is similar to that in the rest of the series.

[Compare the previous abstract, No. 409.]

N. Alders

411. **Structure of the Chorionic Villi in Prolonged Pregnancy.** (Sulla struttura dei villi coriali nelle gravidanze protratte.)

By M. GIARDINELLI. *Minerva ginec., Torino*, **8**, 419–427. May 30, 1956. 1 table. 12 plates. 19 refs.

It is generally conceded that undue prolongation of pregnancy occurs and carries a risk to the foetus. Part of this risk is commonly attributed to senescence of the placenta leading to reduction in its capacity to supply the foetal needs for oxygen and other materials. This placental senescence is held to be demonstrable by infarction, calcification, arterial sclerosis and degenerative changes in the chorionic villi, especially in the syncytial layer cells. The author examined chorionic villi from the placentae of 35 women who had gone from 14 to 36 days beyond the calculated term, and compared them with villi from placentae of the last trimester of normal pregnancies, noting in each case any evidence of foetal anoxia or other adverse foetal condition. The villi selected for examination were taken both from central and peripheral areas of the placenta but avoided places where infarction was evident. He found there was no constant relationship demonstrable between degenerative changes found in the villi in these cases and foetal manifestations, and that in some cases of severe postmaturity marked changes in the villi may be absent. Similarly degenerative changes in the villi can be well marked without apparent harm to the foetus. (This last finding could more easily occur where there is no delay or complication in the process of labour.)

W. C. Spackman

412. **Tuberculosis and Pregnancy.**

By L. M. ROSENBACH and C. R. GANGEMI. *J. Amer. med. Ass.*, **161**, 1035–1038. July 14, 1956. 3 refs.

Prior to the year 1850 medical opinion held that pregnancy had a favourable effect on tuberculosis. For the next 74 years a complete reversal of opinion occurred, so that therapeutic abortion was frequently advised because of the supposed deleterious effect. Since about 1924 the concept that pregnancy itself exerted neither a favourable nor an unfavourable effect on tuberculosis has gained increasing support.

The authors studied the course of pulmonary tuberculosis in 152 patients who underwent 241 pregnancies in a 30-year period from 1925–1954 and who were under the care of the Henry Phipps Institute, University of Pennsylvania. The cases were classified as minimal tuberculosis (101), moderately advanced (109), and far advanced (31).

In the entire series 19 cases showed retrogression and only 23 cases showed progression of the disease. Of the 23 progressive cases 20 either had inadequate treatment or refused treatment altogether. Therapeutic abortion

was performed 19 times but 4 of these cases became worse during the ensuing year and no evidence of benefit from the procedure was obtained. It is concluded that with adequate and proper present-day management of tuberculosis pregnancy should not be considered as a complication.

D. W. James

413. **Bicornuate Uterus: A Report of Five Cases in Late Pregnancy.**

By L. G. R. VAN DONGEN. *S. Afr. med. J.*, **30**, 659–661. July 14, 1956.

Various types of uterine and vaginal anomalies are found in 0·1 per cent to 0·15 per cent of pregnant women. Only in marked cases of arrested development is pregnancy impossible. In the milder forms the abortion rate is very high.

The term "bicornuate uterus" should be used to denote the uterus arcuatus and the uterus bicornis unicollis. There is no doubt that many cases are never diagnosed.

Five cases are described in detail. All the patients were delivered within a 3-months period at the Queen Victoria Hospital, Johannesburg. Two of the patients were primiparae, and both had vertex presentations. The upper poles were not in the midline, and soft globular masses could be felt on the opposite side of the abdomen.

The other 3 patients were multiparae, and all had breech presentations. Each patient had had one previous full-time pregnancy. In 2 cases this had been complicated by an oblique lie, and the third patient had had a persistent breech presentation. In all 3 cases external cephalic version failed, although it seemed that it would be easy in each case.

One of the patients had a congenital heart lesion. In no case was there evidence of congenital defect in the renal system. Three of the 5 cases had unfavourable pelves, a feature which the author thinks has not been reported as a concomitant of bicornuate uterus.

L. J. Abramowitz

414. **Advanced Extrauterine Pregnancy: Clinical Aspects and Review of Eight Cases.**

By C. YAHIA and G. MONTGOMERY. *Obstet. Gynec.*, **8**, 68–80. July 1956. 2 tables. 2 figs. 28 refs.

Eight cases of extra-uterine pregnancy of 5 months or over occurring at the Sloane Hospital for Women, New York, during the period 1932–55 represent an incidence of 1 in 8,550 viable deliveries. There were no maternal deaths and the foetal mortality was 62·5 per cent. All 8 cases were negroes and in most there was a history of infertility. Diagnosis is often difficult. A history suggesting tubal abortion or rupture is common and the condition was primarily a tubal gestation in at least 6 of the 8 cases. Six of the cases had recurrent, crampy, abdominal pain throughout pregnancy and 7 had early, intermittent, vaginal bleeding. The so-called pathognomonic signs of superficiality of foetal small parts, unusually loud foetal heart and inability to palpate the round ligaments are infrequently found. The foetus usually lies abnormally high in a transverse position. Nodularity in the recto-vaginal pouch was felt in 3 cases. The uterus is usually enlarged and considered to be a second abdominal mass separate from the larger gestational sac. It may be mistaken for fibroids, a bicornuate uterus or an ovarian cyst. The cervix is usually firm, long, closed and tucked behind the symphysis or up against the sacrum.

X-ray investigation is frequently helpful. There may be no uterine wall shadow surrounding the foetus which has commonly a transverse lie. The uterus may appear as a soft tissue density in the pelvis. Foetal parts may lie posterior to the lumbar vertebrae in a true lateral film of the abdomen. A lithopaedion may be recognizable.

If the foetus is alive, operation can be delayed to 36–38 weeks. There is no general agreement as to whether or not it is wise to delay laparotomy if the foetus is dead to allow the placental site to become less vascular. The placenta should be removed if this can be done easily. If it is closely adherent to bowel or major vessels, it should be left untouched and the abdomen closed without drainage. Hysterectomy is often necessary.

Congenital deformities of the foetus are frequent and occurred in 2, possibly 3, of the authors' cases.

J. G. Dumoulin

415. **Co-existing Intra-uterine and Extra-uterine Pregnancies.**

By H. JUDELMAN. *S. Afr. med. J.*, **30**, 663–664. July 14, 1956.

The author describes a case of a 36-year-old Bantu female who had given birth to a normal full-term live infant 6 weeks previously. She looked ill, was pale and the abdomen was markedly distended. Laparotomy following paracentesis revealed an extra-uterine pregnancy. The foetus was 10 inches long and weighed 2½ pounds. Recovery was uneventful.

L. J. Abramowitz

LABOUR

416. **Antiseptics in Midwifery.**

By R. M. CALMAN and J. MURRAY. *Brit. med. J.*, **2**, 200–204. July 28, 1956. 6 refs.

The authors, from the Bernhard Baron Memorial Research Laboratories, Queen Charlotte's Maternity Hospital, have undertaken a series of experiments to determine, in their opinion, the most suitable antiseptic for midwifery at present. Six antiseptics were used—their trade names being Hibitane, Bradosol, Octaphen, Dettol, Cetavlon and Roccal.

All antiseptics were tested against four standard organisms—*Ps. pyocyanea*, *Bact. coli*, *Staph. pyogenes* and Group A β-haemolytic streptococcus. Two methods were used for each antiseptic. In the first, a constant dose of organisms was exposed to varying dilution of antiseptic in broth or blood broth for 48 hours at 37° C. In the second a standard inoculum was exposed to varying concentrations of antiseptic for intervals of 2½, 5 and 30 minutes. As little difference was found after these varying times, it was decided to report only results after 2½ minutes.

The more promising antiseptics were also tested by

different techniques against several strains of *Cl. welchii* and *Cl. tetani*.

All the newer antiseptics showed a useful level of activity with high dilution. Hibitane seemed the most effective and Dettol the least in this respect. Tests with *Cl. tetani* showed that some spores could survive the action of all these antiseptics at low dilution, and the authors emphasize the necessity of autoclaving all pads and dressings.

With *Cl. welchii* the 48-hour tests were satisfactory, but not the 2½ minute contact—emphasizing again the need for careful obstetric and operative technique. The amount of soap used in scrubbing up was not felt to be sufficient to affect the bactericidal activities of these antiseptics.

An antiseptic for use in a maternity unit must not only be efficient, but also relatively inexpensive at the necessary dilution. It must be non-toxic, and with a wide margin of safety. It must be active in the presence of fresh blood. The authors have used Hibitane for two and a half years and feel it is the most satisfactory antiseptic at present. They recommend the following strengths: 1/2,000 as a liquid solution; 1/100 as an obstetric cream and a hand cream; a 1/200 solution containing 70 per cent industrial spirit for skin preparation and instrument storage. They recommend rubbing in 1 per cent Hibitane hand cream after scrubbing up, prior to putting on sterile gloves. *Eileen Wilson*

417. **Labour after Psycho-physical Preparation.** (Il parto naturale con il metodo psico-fisio-terapico. Fondamenti teorici e resultati clinici.)

By A. Bocci, G. Chiaudano, L. Davitti, G. Pinoli, and I. Terzi. *Minerva ginec., Torino*, **8**, 453–497. June 15, 1956. 16 figs. 400 refs.

This is a continuation and sequel to the article on the same subject already abstracted (*J. Obstet. Gynaec. Brit. Emp.*, 1956, **63**, 613). The course of preparation at which the women are asked to attend consists of 8 talks with films and 14 to 18 sessions for physiotherapy. The full programme of the lessons and an indication of the cartoon-type films is given. The course has become so popular that a special centre has been established at the University Clinic at Turin and attendance has gone up in one year from seven to a hundred and eight. The results as regards the course of labour appear to justify the enthusiasm of the organizers.

[It may be felt that the method demands a strong and continuous control by an enthusiastic team in order that the co-operation of the individual women, on which the whole success of the plan depends, can be captured and retained. Without this the scheme would not be acceptable to the more independent patients of British hospital departments.]

W. C. Spackman

418. **Trial Labour as an Obstetric Procedure.**

By J. Miller. *S. Afr. med. J.*, **30**, 649–650. July 14, 1956.

The author states that his aim is to assess the value of trial labour in present day conditions.

The various factors not known until labour is in progress are discussed. He asks whether one should not interfere earlier in cases of postmaturity because of rigidity of the foetal skull and possible placental insufficiency. Also should a history of threatened abortion preclude trial labour on account of probable placental insufficiency? Foetal and maternal distress should be anticipated, and the trial concluded before this occurs.

Vaginal rather than rectal examination is preferred. This should be performed early in labour, as presentation of the cord is then much less likely to be missed. With the usual aseptic precautions and chemotherapy this is not thought to be harmful. Vitamin K should also be administered early in labour. An intravenous drip in the later stages of labour and prophylactic forceps may well alter the prognosis.

Induction of labour may be indicated in the next pregnancy, and if it is, the author coins the maxim "Once a trial labour, always a trial labour".

A case is reported of a 28-year-old Bantu primigravida, married for 11 years and treated for infertility. Labour progressed satisfactorily until full dilatation. The foetal heart then disappeared due to presentation of the cord. This complication had not been appreciated on rectal examination.

There is no second chance for failed trial labour patients. Elective Caesarean section should be performed in a subsequent pregnancy.

L. J. Abramowitz

419. **Pelvic Bony Dystocia.**

By D. F. Kaltreider. *West. J. Surg. Obstet. Gynec.*, **64**, 411–414. July 1956.

The author, from the University of Maryland, points out that the rachitic flat pelvis is becoming rarer while there has been an increase in the frequency of transverse contraction of the pelvic brim. Clinical diagnosis of pelvic contraction is difficult but it should be expected when the pubic arch is narrow and the bony structure heavy. Narrowing of the sacroscratic notch and prominence of the ischial spines are also danger signs. X-ray pelvimetry is helpful, the ideal time being at the onset of labour, but failing this, within 10 days of the estimated date of confinement. All coloured patients should be examined as in them the incidence of contraction approaches 10 per cent. The author adopts Mengert's indices for prognosis: the anteroposterior diameter of the inlet multiplied by the transverse diameter of the inlet should exceed 123 sq. cm., and the product of the interspinous and anteroposterior diameters of the outlet should exceed 106 sq. cm. All patients who have a vertex presentation with inlet contraction deserve a trial of labour; care must be taken to maintain adequate fluid balance and wide range antibiotics should be given as prophylaxis against intra-uterine infection. If the patient has normal uterine contractions and the membranes remain intact she is allowed to go to full dilatation; if the head comes down one can expect vaginal delivery. If the head is still high and mobile, the membranes are ruptured, and the patient watched for half an hour; if the head does not now descend,

Caesarean section is performed. If there is uterine inertia, either primary or secondary, Caesarean section is the better part of valour. With midplane contraction and inertia, Caesarean section is indicated. With normal contractions, however, labour is allowed to progress to full dilation; descent of the head can be checked by a lateral X-ray, and care should be taken not to apply the forceps too soon. Positional abnormality may be corrected by rotation, the patient being given a regional block anaesthetic, and the forceps applied, care being taken during the rotation to avoid damage to the foetal skull. The author considers that the outlet and midplane should be considered as one unit.

The commonest abnormal presentation is the breech, and all these patients should have an X-ray pelvimetry. The decision for vaginal or abdominal delivery should be made before or at the onset of labour. Criteria for Caesarean section are contraction of the pelvis, poor pelvic shape and oversized infant; any two are sufficient indications. Other abnormal presentations should be managed by Caesarean section unless the foetus is small or dead.

D. C. A. Bevis

420. **Oxytocic Action of Dihydroergotamine.** (Oxytocische Wirkung von Dihydroergotamin.)

By W. C. CHRIST. *Gynaecologia, Basel,* **141,** 224–227. Apr. 1956.

The author describes the results of his uterine tocographic experiments at Zürich with dihydroergotamine:

(1) Twelve antenatal patients, varying from a few to 52 days before term, were given 0·25 mg. dihydroergotamine (D.H.E.) intramuscularly. In all, the uterine contractions increased in frequency and some of the patients went into labour, the earliest after 4 hours.

(2) During the first stage of labour when 0·25 mg. D.H.E. was given intramuscularly, after 15 minutes the uterine contractions increased in frequency but the uterine tone was reduced in all cases. In one case the foetal heart slowed temporarily but rapidly returned to normal.

Three patients in labour with a dead foetus were given 1 mg. D.H.E. intravenously. Immediately the contractions increased in frequency: in 2 cases the tone was unaltered, and in 1 the uterine tone increased.

(3) Ten patients were given 0·25 mg. D.H.E. intramuscularly within one hour of the delivery of the placenta. The frequency of the uterine contractions diminished in 5 cases, remained the same in 3 and increased in 2. The uterine tone was unchanged in 6 cases and reduced in 4.

(4) Dihydroergotamine was given in various dosages to puerperal women 2–6 days after delivery.

An intramuscular injection of 0·25 mg. D.H.E. caused an immediate slight increase in the frequency of the uterine contractions; half showed reduced tone, the rest no change. Repeat tests four hours later showed that the tone as well as the frequency of uterine contractions has increased.

Within two minutes of receiving an intravenous injection of 1 mg. D.H.E. the uterine contractions increased in frequency, the tone also increased in most, although in one there was a diminution. 0·25 mg. D.H.E. intravenously gave similar results after an interval of 3–5 minutes. Four hours later 7 of 10 patients tested showed more frequent uterine contractions, and in all the uterine tone had increased.

[The author omits to state the number of patients tested during labour, and does not mention the subsequent course of the labour. He stresses the late effect of dihydroergotamine but draws no conclusion. A lively discussion after the paper, however, supports the use of 0·25 mg. dihydroergotamine by intramuscular injection to induce labour, especially after the membranes have ruptured and, also, its value to hasten a prolonged first stage, particularly when contractions are infrequent. The fact that the small intramuscular dose of dihydroergotamine invariably reduced the tone of the uterus in labour, is of great interest.]

Jean L. Hallum

421. **Induction-Delivery Interval Following Artificial Rupture of the Membranes.**

By G. A. MANLY. *Lancet,* **2,** 227–229. Aug. 4, 1956. 9 refs.

The author analyzes the results of 500 cases of artificial rupture of the membranes. Sixty patients had the forewaters ruptured as a primary procedure and 393 patients had a successful hind-water rupture. The remaining patients had a failed hind-water rupture necessitating fore-water rupture. The main indication for the induction of labour was postmaturity which accounted for 65 per cent of the cases, and the next commonest indication was toxaemia (18·5 per cent). There were 24 cases of surgical induction for ante-partum haemorrhage. Anaesthesia was only used in cases of ante-partum haemorrhage and in the very nervous patient. The author considers that the question of whether a head or breech presents is unimportant and that a mobile head is no contra-indication to rupture of the membranes. Prolapse of the cord occurred only once and hence is considered a rare complication. The quantity of liquor removed bore no relation to the induction-delivery interval. The more dilated the cervix at the time of induction the sooner labour ensued, but the closed hard cervix is considered to be no contra-indication to puncture of the membranes.

H. H. Fouracre Barns

422. **Artificial Ripening of the Cervix by Intravenous Pitocin.** (Maduracion artificial del cervix por pitocin intravenoso.)

By L. CASTELAZO AYALA. *Obstet. Ginec. lat-amer.,* **13,** 496–501. Dec. 1955. 2 tables. 20 refs.

Because surgical induction of labour by rupturing the membranes is frequently unsuccessful in those cases in which the cervix is not taken up, the author has devised the practice of giving an intravenous pitocin drip in order to take up the cervix prior to rupturing the membranes. The method used is to give Demerol 100 mg. intramuscularly, and 15 minutes later set up an intravenous drip of 0·2–0·5/1,000 solution of pitocin, at the rate of 10–20 drops a minute.

This is given for 6–9 hours. He then waits for 24–48

hours, and if a vaginal examination reveals no change in the cervix, the drip is repeated. But if the cervix has taken up, the membranes are ruptured and an intravenous drip of a 1/1,000 solution of pitocin is set up.

Surveying the results of 46 cases (18 of whom were nulliparous) in patients between the 16th and 36th weeks of pregnancy the author states that only 2 cases failed to respond. One case was a rapidly progressing toxaemia of pregnancy upon whom a Caesarean section had to be performed, and the other patient refused the second intravenous drip.

The author concludes by stating that the age of the gestation is of no significance. There were no still-births, but one neonatal death occurred in a premature baby from a pre-eclamptic mother.

John F. Foulkes

423. **Interlocked Twins: A Case Report and Brief Review of the Literature.**

By R. GORDON. *S. Afr. med. J.*, **30**, 661–663. July 14, 1956. 4 figs. 13 refs.

The author states that the incidence of locked twins is 1:1,000 twin deliveries or 1:90,000 of all deliveries.

A case is described of a 19-year-old Bantu female, a gravida-2. An unassisted breech delivery of the first twin was partially accomplished, including delivery of the arms. Delivery of the head failed. On examination the head of the second twin was found to be engaged in the pelvis, with an arm alongside the head. The head of the first twin was palpated in the right iliac fossa. Attempts at disimpaction failed, and as both babies had died at that stage the head of the second twin was perforated. This was followed by downward traction of the first twin and perforation of the aftercoming head. The babies weighed 5 pounds 6 ounces and 5 pounds respectively.

The author describes the 4 main ways in which interlocking may occur. The predisposing factors are small foetuses, an unduly roomy pelvis, oligohydramnios, mono-amniotic twins, and extension of the leading head. Of 28 cases reviewed in 1907, 23 were in primigravidae. The mortality of the leading twin is nearly 60 per cent.

Caesarean section will offer the greatest chance of success, but treatment is often prejudiced by late diagnosis, in which case some form of destructive operation is preferable. The unique method described by Kimball and Rand (*Amer. J. Obstet. Gynec.*, 1950, **59**, 1167) is described. The breech is held up by the extremities and Piper forceps applied to the head of the second twin. After delivery of the head of the second twin simultaneous delivery of both twins is effected by manual traction.

L. J. Abramowitz

424. **Ruptured Uterus.**

By H. F. BURKONS. *Obstet. Gynec.*, **7**, 675–683. June 1956. 11 refs.

This is a survey of 65 cases of uterine rupture from hospitals in Ohio. In 35 cases the aetiological factor was a previous Caesarean section, and it has been suggested that rupture occurs in 2 to 4 per cent of vaginal post-section deliveries. From his own series of 35 cases, the author considers that the individual patient with ruptured uterus takes the following risks: (*a*) losing her life—2·8 per cent, (*b*) losing her baby—51·4 per cent, (*c*) losing her uterus—41 per cent. Rupture occurred in 29 cases following classical section and in 6 following lower cervical section.

In 7 of the 65 cases (10·8 per cent) rupture occurred during delivery with 1 maternal death. Internal podalic version accounted for 2, neglected transverse lie 1, and traumatic delivery 4. In 5 cases posterior pituitary extract precipitated uterine rupture with 2 maternal deaths. Excessive multiparity was of aetiological importance in 4 cases and disproportion in 3 cases. Three ruptures were due to traumatic accidents by a severe blow on the abdomen.

In the series of 65 cases there were 7 maternal deaths (10·8 per cent), only 1 of them occurring in the previous section cases. There was a foetal loss of 61·5 per cent.

J. G. Dumoulin

425. **Rupture of the Uterus with Special Reference to Aetiology and Treatment.**

By K. DASGUPTA. *J. Obstet. Gynaec. India*, **6**, 371–379. June 1956. 17 refs.

The author briefly reviews recent literature on the subject, and describes 16 personal cases collected over a 4-year period in a hospital in India. The incidence was 1 in 1,800 deliveries. This is compared with the incidence of approximately 1 in 3,000 in Philadelphia, and 1 in 95 in Peiping.

Complete rupture extending into the peritoneal cavity, was more common than the incomplete variety, but many incomplete ruptures may have been missed and diagnosed as obstetric shock. Seven of the cases had previously had a classical Caesarean section, 1 had a previous manual removal of the placenta, and in 1 case spontaneous rupture occurred at the site of a posterior placenta praevia. Five cases were associated with obstructed labour. In 2 cases, the cause of rupture was not known. Such cases, especially if occurring before labour, were thought to be due to hyaline and fatty degenerative changes in the uterine wall in multiparous women.

The importance of unrecognized hydrocephalus as a cause of spontaneous rupture in labour is emphasized, while internal version is the most usual cause of traumatic rupture. An "occult rupture" with slightly atypical symptoms, may result in delay in diagnosis and treatment, and the author mentions supra-pubic pain, unexplained maternal tachycardia, and unexplained intra-partum or post-partum haemorrhage as reasons for suspecting rupture.

The maternal mortality was 32·5 per cent. Two cases were moribund on admission. Of the remaining 14, all were operated on, and 4 died. The causes of death were post-operative shock, unsuitable blood transfusion, peritonitis, and intestinal obstruction. Early laparotomy is thought to be an important factor in treatment. If rupture occurs in labour, even in the terminal stages,

delivery by the vagina is contra-indicated, as it delays laparotomy and may introduce sepsis. In 8 cases, the rent was sutured and the patient sterilized. Hysterectomy, total or sub-total, was done on the remaining 6 cases which had operative treatment. The foetal mortality was 62 per cent.

John McKiddie

426. **Coagulation Defects in Severe Intrapartum and Postpartum Hemorrhage.**

By D. E. Reid, C. C. Roby and A. E. Weiner. *J. Amer. med. Ass.*, **161**, 1244–1247. July 28, 1956. 14 refs.

Blood loss is still a major factor in maternal deaths and under certain circumstances blood transfusion alone fails to stabilize the patient's condition. Coagulability of the blood becomes defective (fibrinogen content less than 100 mg. per 100 ml.) particularly in cases of severe premature separation of the placenta, after foetal death *in utero*, and as a secondary effect of amniotic fluid embolism. Originally referred to as afibrinogenaemia, the term hypofibrinogenaemia is now thought to be more appropriate for the condition. Although the aetiology is uncertain the authors have demonstrated the presence of fibrinolysin in the blood of patients with hypofibrinogenaemia although they have not been able to determine its origin.

The majority of cases occur in association with severe premature separation of the placenta. It has not been seen in the milder cases, and only in association with foetal death *in utero* when the foetus has been retained for more than five weeks. It is rarely encountered before the 20th week of pregnancy. A suitable bedside test for hypofibrinogenaemia involves only the withdrawal of 5 ml. of the patient's blood into a clean dry test tube. Normal blood will clot within 8 to 12 minutes and the clot will remain intact for 24 hours. In hypofibrinogenaemia the blood may not clot and if it does so may undergo dissolution within 30 to 60 minutes.

In premature separation of the placenta delivery per vaginam is preferable, and even if Caesarean section is necessary the important principle of treatment is to restore the coagulability of the undelivered patient's blood to normal by the administration of blood and fibrinogen. The average case requires 1,500 to 2,000 ml. of blood and 4 to 8 g. of fibrinogen. Two case histories are given illustrating this treatment.

D. W. James

427. **Chlorpromazine in Normal Labour.**

By W. B. Harer. *Obstet. Gynec.*, **8**, 1–9. July 1956. 9 tables. 2 refs.

The effect of chlorpromazine in 500 normal women in labour is compared with a control group of 500 cases. The dose used was 50 mg. initially. When used alone chlorpromazine produces considerable drowsiness but no amnesia. It modifies the action of barbiturates and potentiates the action of pethidine. It makes patients in labour more co-operative, more alert and quieter. It produces marked hypotension in 18 per cent of cases. It reduces the amount of nausea and vomiting. It has no harmful effect on either mother or foetus.

The author concludes that the drug is useful in the relief of pain in labour in selected cases.

J. G. Dumoulin

MATERNAL MORTALITY AND MORBIDITY

428. **Maternal Deaths from Obstetric Anesthesia and Analgesia: Can They Be Eliminated?**

By C. S. Stevenson, H. A. Ott, P. E. Sutton and M. L. Byrd. *Obstet. Gynec.*, **8**, 88–98. July 1956. 6 tables. 7 refs.

In Michigan, the authors have estimated that there is 1 maternal death from obstetric anaesthesia in every 20,500 births, or 1 death in every 16,000 obstetric anaesthesias. Whilst this figure is low, 25 of the 34 reported deaths could have been avoided. Sixty per cent of the deaths were accounted for by spinal anaesthesia and 23 per cent by inhalation anaesthesia. Excessive dosage, improper technique, and its use when contra-indicated were the main lethal factors in the spinal group. In the inhalation group, they were anoxia, aspiration of vomit and cardiac arrest.

Pudendal-nerve-block anaesthesia is adequate for the majority of vaginal deliveries and seems the safest method of all to use. Local infiltration is the safest for Caesarean section.

The lowering of maternal deaths from anaesthesia to the irreducible minimum would prevent 5 to 10 per cent of all maternal deaths.

J. G. Dumoulin

429. **Puerperal Tetanus: Treatment with Muscle-Relaxants and Assisted Respiration.**

By A. M. Ramsay, E. M. France and B. M. Dempsey. *Lancet*, **2**, 548–550. Sept. 15, 1956. 15 refs.

From the literature it appears clear that the use of muscle-relaxant drugs, coupled with tracheotomy and assisted respiration, has brought a considerable improvement in the prognosis of tetanus. The authors record a further case of puerperal tetanus following abortion which was successfully treated in this manner. Intravenous "Scoline" was the muscle-relaxant used and was given for 10 days. During this time respiration was assisted by a Beaver Mark II respirator through a shortened cuffed endotracheal tube which was inserted through a low tracheotomy. Tetanus antitoxin, penicillin and sedatives were also given. Feeding of the patient was carried out by intravenous fluids and gastric feeding. Under cover of further antitoxin the uterus was evacuated of the remains of the infected placenta on the eleventh day after admission. The tracheotomy wound was healed by the 32nd day and the patient discharged on the 46th day.

H. H. Fouracre Barns

430. **Puerperal Breast Abscess. II. Epidemiological Factors in Hospital-Acquired Infection.**

By A. J. Sherman, H. C. Porter and G. M. Eisenberg. *Obstet. Gynec.*, **8**, 81–87. July 1956. 6 tables. 16 refs.

This is the second part of a report on an outbreak of staphylococcal breast abscesses among patients delivered in Philadelphia General Hospital. Coagulase-positive staphylococci were isolated from 13 breast abscesses in 12 of which penicillin-resistance was demonstrated. The authors show that there is a higher incidence (12 per cent) of asymptomatic penicillin-resistant staphylococcal infection among hospital personnel compared to the incidence of the organism among the population at large, suggesting that puerperal suppurative mastitis may well be a hospital-acquired infection. An analysis of the phage patterns of the organisms suggests that the staphylococci inhabiting Philadelphia General Hospital are different from those of the community at large.

J. G. Dumoulin

OBSTETRIC OPERATIONS

431. **Post-Cesarean Obstetrics.**

By S. J. BIRNBAUM. *Obstet. Gynec.*, **7**, 611–618. June 1956. 9 refs.

For over 20 years it has been the policy of the New York Lying-In Hospital to individualize the mode of delivery of patients who have had a previous Caesarean section. In general, patients are given the opportunity of vaginal delivery if the conditions prompting the previous section no longer exist. In labour they are carefully watched and blood is always available. The second stage is usually shortened by forceps delivery. The uterine cavity is explored after delivery of the placenta for defects in the myometrium. The risk of rupture is approximately 1 per cent. If it occurs, it is less catastrophic than a spontaneous rupture since the area of the scar is relatively avascular.

The number of sections performed for the indication "previous Caesarean section" has increased from 23 per cent in 1950 to 42 per cent in 1954. Repeat section was performed in 80·6 per cent of the private patients and 49·3 per cent of the ward patients in 210 cases (1953–54). There was 1 maternal death from air embolism.

Important factors in determining the route of delivery are previous vaginal delivery, the number of previous sections and the adequacy of the pelvis. In patients in whom trial of labour failed, the failure was not related to the previous section but to other factors necessitating a section in their own right. The type of section previously done is probably not very important.

The incidence of myometrial defects was 5·8 per cent with 1 complete rupture of a classical scar. The author believes that there is more risk to foetus and mother from routine elective section than from uterine rupture.

J. G. Dumoulin

INFANT

432. **The Effect of Season of Birth on Neonatal Growth in South African European and Coloured Babies.**

By E. J. SALBER. *S. Afr. J. Lab. clin. Med.*, **2**, 160–167. June 1956. 6 refs.

The author has studied the records of 906 European and 344 coloured babies born in the Addington Hospital, Durban, from 1st May, 1951 to 30th April, 1952. The effect of season on (1) the total initial loss of weight and (2) the duration of that loss, is assessed.

In both groups there was a greater loss of weight in the winter than in the summer months. This was statistically significant. There was a loss of weight for a longer period in the winter months, but the differences were not significant. Both groups were studied separately, and in the European group males and females were studied separately. The trend throughout was the same, although the loss of weight was slightly greater in the females than in the males.

L. J. Abramowitz

433. **Survival in Infancy: A Comparative Study of Stillbirths and Infant Mortality in Certain Zulu and Hindu Communities in Natal.**

By S. L. KARK and J. CHESLER. *S. Afr. J. Lab. clin. Med.*, **2**, 134–159. June 1956. 27 refs.

The authors have analyzed the stillbirth, neonatal and post-neonatal (1–12 months) mortality in 3 Bantu (predominantly Zulu) and 2 Indian (predominantly Hindu) communities.

	Live Births	Still-Births	Neonatal Deaths	Post-neonatal Deaths	Total Infant Mortality
ZULU					
Rural Native Reserve:					
"Early period"	794	35 (4·2)	48 (6)	105 (13·2)	153 (19·2)
"Late period"	1,180	61 (4·8)	50 (4·2)	92 (7·7)	142 (11·9)
Urban Slum ..	340	18 (5)	15 (4·4)	28 (8·2)	43 (12·6)
Urban Municipal Housing Project	693	23 (3·2)	24 (3·4)	28 (4)	52 (7·5)
HINDU					
Urban Slum ..	276	9 (3·1)	2 (0·7)	13 (4·7)	15 (5·4)
Urban Municipal Housing Project	705	15 (2·1)	9 (1·2)	25 (3·5)	34 (4·8)

Percentages in parentheses.

The striking difference between the 2 groups is the surprisingly low Hindu neonatal death rate. In the Zulu communities the "rural" post-neonatal death rate is much higher than in either of the urban groups. This improved markedly in the "late period", when medical facilities became available.

The various factors are discussed. As a rule there was slightly less crowding in the Zulu urban areas than in the Hindu areas, and the Zulu income was a little higher. The standard of formal education of the Hindu women was very much lower than in any of the 3 Zulu groups.

Water supplies and lavatory provision were very unsatisfactory in all but the municipal housing projects.

Maternal ages and birth ranks are compared.

There were very many more illegitimate Zulu than Hindu babies. In the Zulu groups there was no difference in the infant mortality rates of legitimate and illegitimate children.

More Zulu than Hindu mothers had skilled antenatal attention and skilled midwifery services. Hindu mothers preferred semi-skilled domiciliary care over a longer period.

The incidence of syphilis was:

Hindu	1·0 per cent
Zulu:	
(1) Rural	23·2 per cent
(2) Urban slum	24·0 per cent
(3) Housing project ..	12·5 per cent

It is concluded that the well-established associated factors do not in themselves explain the differences found between the Zulu and Hindu groups.

L. J. Abramowitz

434. **Perinatal Mortality: Clinical and Pathologic Aspects.**

By R. E. L. Nesbitt and G. W. Anderson. *Obstet. Gynec.*, **8**, 50–60. July 1956. 6 tables. 11 refs.

There were 26,776 infants weighing 1,000 g. or more delivered at the Johns Hopkins Hospital over the years 1937–49. The perinatal mortality was 1,043 (3·8 per cent) made up of 312 deaths *in utero* before labour (30 per cent), 255 deaths during labour (24 per cent) and 476 neonatal deaths (46 per cent).

The incidence of prematurity (infants less than 2,500 g.) was 11·2 per cent and in this group were 566 deaths. Of the 23,768 infants weighing 2,500 g. or more at birth, the mortality was 477 (2 per cent).

In the whole series, the cause of death was classified as follows: Anoxia 33·7 per cent, no obvious abnormality 32 per cent, birth injury 9·8 per cent, malformation 9·4 per cent, abnormal pulmonary ventilation (hyaline membrane) 7·1 per cent, infection 5·6 per cent, erythroblastosis 1·6 per cent, and other conditions 0·8 per cent.

In the anoxia group, abruptio placentae was the commonest pathological state responsible for deaths.

J. G. Dumoulin

435. **Neuropsychiatric Sequelae of Prematurity.**

By H. Knobloch, R. Rider, P. Harper and B. Pasamanick. *J. Amer. med. Ass.*, **161**, 581–585. June 16, 1956. 10 refs.

The relationship of prematurity to foetal and neonatal death is unquestioned, but the course of development and adjustment of those premature infants who survive is not so clearly defined. The authors, from the Division of Maternal and Child Health, Johns Hopkins University, compared the physical and mental status of 500 single born premature infants with 492 infants born at term. The comparison was made at 40 weeks of age for the full term infants and at the corresponding corrected age for the premature infants. Factors such as race, season of birth, parity of mother, hospital of birth and socio-economic states were taken into consideration.

The examinations were all done by an experienced paediatrician and consisted of a physical examination and a Gesell development examination. The integrity of the nervous system was assessed by the presence or absence of impairment in neuromotor functioning and deviations in muscle tonus and control. After a complicated mathematical analysis of all the factors involved the incidence of abnormalities was found to increase as the birth weight of the infant decreased, so that 50·9 per cent of the infants with a birth weight of less than 1,501 g. (3·3 pounds) had defects ranging from minor neurological damage to severe intellectual deficiency. The adjusted percentage of premature infants showing some departure from normal development was 25·7 per cent compared to 12·8 per cent of the full term controls.

The authors discuss the value of the tests at nine months of age and they have already examined about 250 of the cases again at three years of age. Final results will be presented in a later communication, but the results of the present study already indicate that the methods described are effective in picking out infants in need of supervision.

[Survival of the premature infant is more common today with expert paediatric care, but these figures introduce another disturbing aspect of the problem which can only be answered in the field of obstetrics by the prevention of prematurity.]

D. W. James

436. **Influence on the Prothrombin Time of Breast-Fed Newborn Babies of One Single Dose of Vitamine K_1 or Synkavit Given to the Mother within Two Hours after Birth.**

By H. V. Dyggve, H. Dam and E. Søndergaard. *Acta obstet. gynec. scand.*, **35**, 440–444. 1956. 1 fig. 8 refs.

In this paper from Copenhagen it is shown that a single dose of 40 mg. of vitamin K_1 or of synkavit given to the mother within 2 hours after delivery has almost no influence on the prothrombin time of breast-fed infants during the first 2 days; there is, however, a slight improvement on the third day, and a marked improvement on the fourth, fifth and sixth day.

It is concluded that the well-known action of antepartum treatment must be due, at least partially, to vitamin K passing to the foetus through the placenta.

[In the evaluation of these findings it may be useful to keep in mind that the prothrombin level in all infants is at its lowest from 48 to 72 hours after birth.]

N. Alders

437. **The Use of Bioflavonoid Compounds in the Prevention or Reduction in Severity of Erythroblastosis Fetalis.**

By W. M. Jacobs. *Surg. Gynec. Obstet.*, **103**, 233–236. Aug. 1956. 5 refs.

Three factors—prevention or reduction in capillary fragility of the placenta, anti-histamine reaction, reduction or prevention of capillary fragility in the baby—are the basis for the use of bioflavonoid compounds in the treatment of Rh iso-immunized women.

This report deals with 6 cases of previously Rh immunized mothers treated daily from the 14th week of pregnancy with 600 mg. of a bioflavonoid compound (5 other cases were excluded because the babies proved to be Rh negative).

Three patients, although having delivered erythroblastotic babies before, showed no titre rise throughout their pregnancies and the present infants were completely unaffected, as evidenced clinically and by laboratory studies. In 3 other cases base-line titres were present early in gestation, presumably handover anti-

body titres from previous immunization. In all of these the titre rise was only slight and the infants were healthier and less affected than previous ones.

The author concludes that the bioflavonoid compounds do have some value in the prevention or reduction in severity of erythroblastosis foetalis, and similar studies in a larger series of cases are being undertaken.

John P. Erskine

438. **Haemolytic Disease of the Newborn: A Report from the Natal Rhesus Unit.**

By H. L. WALLACE, W. E. B. EDGE, N. M. MANN and P. MOORES. *S. Afr. med. J.*, **30**, 681–686. July 21, 1956. 2 figs. 18 refs.

The procedure adopted at the Natal Rhesus Unit from 1951 to 1955 is described.

Antibody tests are carried out at 24, 32 and 36 weeks. If antibodies develop, admission to hospital is arranged at 38 weeks. Immediately after delivery the following tests are performed on the cord blood:

(1) The direct Coombs anti-human-globulin test.
(2) Haemoglobin estimation.
(3) ABO and Rhesus grouping.
(4) Serum bilirubin estimation.
(5) Normoblast count.

At the same time the obstetrical history is carefully assessed and the infant examined, with special attention to the weight, general health, jaundice and the size of the liver and spleen.

Of 112 pregnancies, 12 terminated in hydrops foetalis, stillbirth or abortion. Among the remaining 100 cases were 20 Rh-negative babies. In 80 babies the Rh and Coombs tests were positive.

The indications for exchange transfusion are discussed. A positive Coombs test should not be the deciding factor, as it is in some clinics. It exposes infants to the risk of operation unnecessarily, and is a waste of precious Rh-negative blood. The standards have been less rigid than in other units, in that the decision for or against treatment has not always depended on pre-elected laboratory findings. For example the haemoglobin level is considered in relation to the many other relevant factors. The ultimate decision has rested on one individual, in an attempt to obtain uniformity of treatment.

Immediate exchange transfusion was performed in 50 cases, and not given in 30 cases. The following factors are considered:

(1) *Birth Weight.* Twelve of the 14 cases whose weight was less than 6 pounds were transfused. One baby died.

(2) *Mother's Obstetrical History.* Sixteen mothers gave a history of one previously affected infant. In 4 of these the new infants were left untreated and made an uneventful recovery. When there have been 2 or more infants affected exchange transfusion should usually be carried out.

(3) *Cord Haemoglobin.* Eleven cases with haemoglobin levels below 15 g. per 100 ml. were left untreated and made good recoveries.

(4) *Serum Bilirubin.* In all the fatal cases the level was above 3 mg. per 100 ml., but 50 per cent of non-fatal cases also had levels above this. Twenty-eight per cent of cases with serum bilirubin levels above 4 mg. per 100 ml. died. If the serum bilirubin rises to 20 mg. per 100 ml. the exchange transfusion should be repeated.

(5) *Coombs Test.* In doubtful cases a strongly positive Coombs test should swing the balance in favour of exchange transfusion.

(6) *The Maternal Antibody Titre.* Of the cases requiring exchange transfusion 45 had a maternal antibody titre of over 64. All the fatal cases, with one exception, belonged to this group.

(7) *The Normoblast Count.* This was a very variable and somewhat unreliable test.

(8) *Splenomegaly.* Of the cases given exchange transfusion 73 per cent had splenomegaly. Twenty per cent of the infants not given transfusion had splenomegaly, mostly of a lesser degree.

The technique of exchange transfusion is discussed.

Of the 50 cases given immediate transfusion, 43 recovered, 6 died and one is suffering from the effects of kernicterus. In the 30 cases not given immediate transfusion 28 recovered and 2 died. Seven subsequently had transfusions. The over-all mortality was 10 per cent. Of the 8 fatal cases 4 had signs of kernicterus before death. Weekly haemoglobin estimations were carried out in all cases of haemolytic disease. Usually there was a steady fall until the 6th or 7th week.

The fatal cases are summarized.

L. J. Abramowitz

439. **Haemolytic Streptococci on the Neonatal Umbilicus.**

By W. KWANTES and J. R. E. JAMES. *Brit. med. J.*, **2**, 576–578. Sept. 8, 1956. 17 refs.

The authors, from the West Wales Area Hospitals, investigated two outbreaks of haemolytic streptococcal infection which have occurred recently. The first occurred in Carmarthen in 1954. Two patients and two nurses were infected. This led to the taking of nose, throat and umbilical swabs from the 13 infants in the nursery. The nose and throat swabs were all negative, but 6 infants carried haemolytic streptococci in the umbilicus.

The second outbreak occurred in Llanelly in 1954. Following the discovery of haemolytic streptococci in the vaginal swab from one mother, umbilical swabs were taken from all nine infants in the nursery. All the umbilical swabs were positive. Investigation showed that without antibiotic therapy these organisms might persist up to 8 weeks after birth. Forty-four infants born at home were investigated. One revealed haemolytic streptococci Group B, one Group C and three with Group D.

The authors stress that the umbilicus of the newborn may provide the means of spread of streptococcal infection to its own mother, to other mothers and infants, to midwives, and in domiciliary practice to other members of the household.

Eileen Wilson

440. Neonatal Umbilicus as a Source of Streptococcal Infections in a Maternity Unit.

By J. M. Boissard and B. Eton. *Brit. med. J.*, **2**, 574–576. Sept. 8, 1956. 5 refs.

The authors investigated an outbreak of streptococcal infection in a maternity ward at the United Cambridge Hospitals. The immediate source of the infection was in the ward nursery. The first incident was the development of puerperal sepsis due to *Streptococcus pyogenes* type 9, in a woman on the sixth day of the puerperium. A midwife became ill at home on the same day with tonsillitis due to the same organism, having been absent from duty the previous two days. It was then found that a swab from the umbilicus from the patient's own infant grew the same organism. Umbilical swabs were taken from all the 20 infants still in the nursery at that time. Five infants showed positive swabs. The organism was also isolated from cots and cot blankets in two cases. The nursery was roomy and accommodated 20 cots. Babies were bathed on the first, fifth and tenth days. The cord was kept bare above the napkin, and treated daily with spirit. Nurses washed their hands between changing the infants but did not use masks, gloves or disinfectants.

It was interesting to note that in most babies, the umbilicus looked normal, even when infected. The authors feel that the infection was introduced into the nursery by some person unknown, but spread via the mothers' or attendants' hands when handling the infants. It is obviously important to investigate the nursery whenever a case of streptococcal infection occurs in a maternity unit.

Eileen Wilson

GYNAECOLOGY

441. Pelvic Arteriography.

By I. Fernström. *Acta obstet. gynec. scand.*, **35**, 164–180. 1956. 11 figs. 1 ref.

This is a study of 550 pelvic arteriographies, coming from the radiological and gynaecological departments of Karolinska Hospital, Stockholm. The technique of puncture of the femoral artery, introduction of a polythene catheter as far up as the abdominal aorta, injection of the opaque medium (40 ml. of a 50 per cent solution of umbradil or of a 60 per cent solution of "urografin"), and radiographic details are clearly described. Apart from a few small subcutaneous haematomata, a few instances of urticaria, nausea and vomiting, and 2 cases of transient disturbance of renal function, no complications were observed.

In 150 cases of fibroids the typical findings were lateral displacement of the uterine artery in its course along the lateral margin of the uterus and loss of tortuosity in this part, and the presence of non-tortuous intramural blood vessels in the vicinity of the tumour.

In 80 cases of intra-uterine pregnancy the uterine artery was generally found to be displaced laterally in its course along the lateral margin of the uterus, between the third lunar month of pregnancy and term. Loss of tortuosity of this part of the artery was observed in addition towards the end of pregnancy in multiparae, and from the beginning of pregnancy in primigravidae. As pregnancy progressed the intramural blood vessels running to the placental sinuses progressively widened; on reaching the sinuses they showed a marked increase in tortuosity. Placental sinuses became opaque from the end of the second month in many, and from the third month until term in all cases. Pelvic arteriography was of special value in cases of suspected placenta praevia.

In 150 cases of adnexal tumours it was found that the tubal or the ovarian branch of the uterine artery was non-tortuous and arched in about one-third of the cases studied. Blood vessels were visible within the tumour in some cases of solid tumour but not in cystic tumours. The diagnosis of adnexal tumour could usually be established but no information was obtained about the nature of the swelling. Pelvic arteriography was of special diagnostic value in cases in which clinical differentiation between adnexal tumours and uterine fibroids presented difficulty.

The method also proved valuable in tubal pregnancy (25 cases): except when the placenta was supplied from the ovarian artery, and in cases of ruptured tubal pregnancy and tubal abortion. But if the blood supply of the placenta was derived from the uterine artery, and if the placenta, or remains of the placenta, were still connected with the blood vessels in the tubal wall, it was found that the tubal wall often gave off several non-tortuous and arched branches, and that the placental sinuses became visible as irregular opacities from the fifth week of pregnancy onwards.

Ten line-drawings illustrate the findings.

N. Alders

442. The Clinical Usefulness of Vulvar Fluorescence for Estimating Oestrogenic Activity.

By D. Trolle. *Acta obstet. gynec. scand.*, **35**, 404–413. 1956. 10 refs.

Margolese (*J. clin. Endocr.*, 1948, **8**, 603) found that irradiation of the external female genital organs with ultra-violet rays brought about purple, yellow, green, brown or red fluorescence of the fossa navicularis, the inner surfaces of the labia minora and the area around the clitoris, and that fluorescence may spread to the labia majora, the perineum, peri-anal region, and in some instances to the inner surfaces of the thighs; no fluorescence was seen on the vagina or the portio vaginalis. This phenomenon is probably a reaction kindred to the colour changes of the sexual skin in monkeys.

The author, writing from 2 hospitals in Copenhagen, found that by testing for fluorescence it was quite possible to "obtain in a quick and simple way an idea of the oestrogenic activity in the women concerned". There was a marked difference in the vulvar fluorescence seen in women of fertile age, and in that of post-menopausal women and castrates. In the latter, the purple fluorescence of women of child-bearing age could be produced by administration of oestrogens, but there was no correlation between the purple fluorescence and the excretion of oestrogens in the urine. There was no difference in the fluorescence of the vulva of pregnant

and non-pregnant women of childbearing age. Oestrogen-producing ovarian tumours may produce purple fluorescence after the menopause.

N. Alders

443. **The Use of Androgens in the Female.**
By G. I. M. Swyer. *Lancet*, **2**, 433–437. Sept. 1, 1956. 8 figs. 5 refs.

The author reports the results of treating women with androgens for various conditions. In cases of regular menorrhagia of which there were 32, androgens alone proved to be of little value but combined with ethisterone were of some help. Regular menorrhagia due to emotional causes (6 cases) did not respond to hormone treatment at all. The results in the treatment of irregular uterine bleeding (12 patients) were unimpressive but help was given in some cases of dysmenorrhoea (5 cases). The symptoms of fibrocystic mastopathy (7 patients) were greatly helped by androgen therapy. There were 5 patients with deficient libido, 4 of whom experienced an increase in libido with androgens. Androgens in combination with oestrogens were of help in 7 "difficult" patients suffering from climacteric symptoms but the author believes that these symptoms are usually treated quite adequately with small doses of oestrogens. For increasing the weight in much-underweight patients (6) androgens proved helpful in some cases. The value of androgens, either alone or in combination with thyroid hormone, for the promotion of growth in children (9 girls) was variable but in some cases quite considerable. The author is careful to point out that the obvious drawback to androgen therapy in the female is its potentially defeminizing and virilizing effects and that it is important to be on the look-out for such undesirable effects.

H. H. Fouracre Barns

444. **Newer Thyroid Preparations. Actions and Usage.**
By P. Starr. *West. J. Surg. Obstet. Gynec.*, **64**, 466–470. Aug. 1956. 13 refs.

The author reviewed the chemistry and pharmacology of various new synthetic thyroid preparations. Patients with ovarian disorders seem to have mild degrees of hypopituitarism and may benefit from 0·05 mg. of desiccated thyroid or thyroxine a day. Pregnant women who need thyroid will require as much as 8 grains (0·9 mg.) of desiccated thyroid a day. Cretins require thyroxine in dosage of 0·025 mg. daily. Benign, non-toxic colloid goitre is best treated by triiodothyronine but the dosage must be fitted to the patient.

D. C. A. Bevis

445. **Ovarian Agenesis with Male Skin Sex. Evidence against Parthenogenesis.**
By R. Platt and F. Stratton. *Lancet*, **2**, 120–121. July 21, 1956. 4 refs.

It occurred to one of the writers that cases of ovarian agenesis might possibly be examples of parthenogenesis. It was thought possible that the male type of nucleus in cases of ovarian agenesis might result not from the presence of a Y chromosome but from the possession of only one X chromosome. The bloods of three patients suffering from ovarian agenesis and the bloods of 2 of the mothers of these patients were investigated and failed to show evidence to support the hypothesis of parthenogenesis having any connexion with ovarian agenesis.

H. H. Fouracre Barns

446. **Colour-Blindness in "Ovarian Agenesis".**
By P. E. Polani, M. H. Lessof and P. M. F. Bishop. *Lancet*, **2**, 118–120. July 21, 1956. 2 tables. 13 refs.

The authors tested the colour vision of 25 cases of "ovarian agenesis" by means of the Ishihara tests. Four patients were found to be colour blind. These results differ significantly from those to be expected from testing a sample of females but not from those to be expected in a sample of males. Hence the results lend support to the hypothesis of the genetic maleness of patients with ovarian agenesis.

H. H. Fouracre Barns

447. **Vaginitis Emphysematosa.**
By F. Zachariae. *Acta obstet. gynec. scand.*, **35**, 393–403. 1956. 6 figs. 57 refs.

This is a clinical and histological description of 2 cases of vaginitis emphysematosa occurring in non-pregnant women which were observed at Bispebjerg Hospital, Copenhagen.

This condition of numerous gas-filled cysts of greatly varying sizes situated in the vaginal connective tissues just beneath the epithelium has been known for almost 100 years. About 100 cases are on record but only 8 of them were observed in living non-pregnant women.

Vaginitis emphysematosa is a misnomer as there is neither inflammation nor true emphysema. The condition is benign and disappears without treatment. It is thus of pathological rather than of clinical interest.

Several theories of its pathogenesis are discussed but the aetiology still remains obscure.

N. Alders

448. **Premenstrual Tension: Review of 288 Cases.**
By R. J. Simmons. *Obstet. Gynec.*, **8**, 99–102. July 1956. 5 tables. 14 refs.

The author reports on 288 cases of severe promenstrual tension seen in his practice. He found that restriction of salt combined with diuretics was useless. Progesterone given in the premenstrual phase was also very unsatisfactory. Testosterone in the premenstrual phase gave satisfactory results in over half of 34 cases so treated, but tended to upset the menstrual cycle; symptoms returned when treatment was stopped in the successful cases.

On the basis of a possible endogenous hormone allergy to progesterone being the cause of premenstrual tension, all cases were tried on oral pregnanediol. Treatment was continued for 3 months and consisted of 0·05 mg. daily. Results were satisfactory in 83 per cent. Recurrence of symptoms, requiring resumption of treatment, was noted in 33 per cent.

J. G. Dumoulin

449. **Cortisone in the Treatment of Infertility.**
By R. B. GREENBLATT. W. E. BARFIELD and C. P. LAMPROS. *Fertil. Steril.*, 7, 203–212. May/June 1956.

Among the most difficult cases of infertility are those patients who are seen not infrequently complaining of delayed, scanty or absent menstruation over a long period, many of these patients being also slightly hirsutic, and on investigation totally anovular. Some of these patients conform to the Stein-Leventhal syndrome with enlarged ovaries, but many do not do so. In the past thyroid and potassium chloride were advocated, together with a high protein and low salt diet, but recently the authors have recorded better results with cortisone. By that is meant that out of 37 patients, 10 have become pregnant and gone to term; whereas 3 more have done so after wedge resection of both ovaries. It would appear that cortisone helps ovulation both during and after its exhibition, possibly by releasing pituitary gonadotropins. The dosage recommended is 25–100 mg. of cortisone acetate daily by mouth, the average dose being 50 mg. per day, for not more than 2 months.

V. B. Green-Armytage

450. **Emotional Factors in Female Infertility.**
By J. P. GREENHILL. *Obstet. Gynec.*, 7, 602–607. June 1956. 29 refs.

The number of women who become pregnant before any therapy is carried out constitutes a high percentage of all supposedly sterile women who attend a clinic for this reason.

Reports from internment camps show that severe psychic shock, fear and worry may cause amenorrhoea. There is undoubtedly a close relation between the hypothalamus and the pituitary gland and the rest of the endocrine system. Several authors have suggested there is a strong psychogenic factor in habitual abortion.

Psychogenic sterility may be due to tubal spasm. A sympathetic physician can do much to help such patients and a psychiatrist may find an emotional basis in many cases of sterility which he can treat.

J. G. Dumoulin

451. **Post Coital Tests During Conception Cycle.**
By A. L. SOUTHAM and L. BUXTON. *Fertil. Steril.*, 7, 133–140. Mar./Apr. 1956.

This is a thought making article founded on 70 post-coital tests done in the Sloane Hospital for Women, New York. The authors classify cervical mucus as good, fair and poor according to the abundance, viscosity, and acellular character of the mucus; good denoting 15 actively motile sperms per high power field. Sixty of the patients were nulliparae and the sterility had ranged from 2–10 years. The tests were of course done at the approximate ovulation period, but despite this it is somewhat remarkable that out of 30 patients who became pregnant, in 12 the mucus was of the poor type, that is it was scanty, viscous, cellular with only an occasional, or sometimes no sperm to be seen. Therefore the prognostic value of the post-coital test is questionable, though it is reported by Buxton that 30 per cent of patients became pregnant within 3 months following good post-coital tests; whereas only 10 followed a poor one.

V. B. Green-Armytage

452. **Some Legal Aspects of Artificial Insemination.**
By A. D. HOLLOWAY. *Obstet. Gynec.*, 7, 621–629. June 1956.

There are 2 types of artificial insemination—with the husband's semen (A.I.H.) and with a donor's semen (A.I.D.). John Hunter was the first person to use it in 1799, and Marion Sims in the United States in 1866. The common law never anticipated such a procedure. The medical profession has developed the technique and the legal profession must adjust it to the welfare of society. If A.I.H., done with the consent of the husband, results in a child being born the law would probably consider the child legitimate. It is A.I.D. which poses the grave questions of legitimacy and inheritance. The medical profession has stipulated that in cases of A.I.D. the husband and not the biological father must be listed on the birth certificate, and the questions of conspiracy and fraud here arise. There are also the problems of adultery and the right of the child to claim support or the right of inheritance from the biological father. In one case in the United States such a child was considered at court to be legitimate and in another illegitimate; it depends much on the definition of adultery.

It is evident that all the parties to A.I.D. are treading on dangerous ground. It is impossible at present to state definitely whether the law will countenance their conduct. The position is made more rather than less complicated by the practice of mixing the semen of the husband and donor before insemination. It is asserted that adoption will provide for the child's rights but this tends to destroy the secrecy which seems so desirable in a case of artificial insemination.

In at least 5 States bills have been presented to legitimize a child born by artificial insemination, but none have come out of the committee for vote of the legislature.

J. G. Dumoulin

453. **Oral Control of Conception.**
By N. MILLMAN and C. G. HARTMAN. *Fertil. Steril.*, 7, 110–122. Mar./Apr. 1956.

It has been computed that the population of the world today of 2·4 billions will be 12½ billions 200 years hence unless some satisfactory international method of contraception is discovered and made compulsory. These staggering figures, which spell such manifest dangers to every country of over-crowding and starvation, compel the scientists of every country to aim at the discovery of some safe and easy method of contraception which would counter the present methods which are so completely useless in the countries where they are most wanted, that is the backward countries. Up to date the antimetabolites, the antienzymes, the antispermatogenics and antihistamines have all been tried with no satisfactory result, though of recent months the botanical preparations, particularly that of India, have given some promise;

but both clover and *pisum sativum*, despite much oriental literature, have not passed all criteria of safety and cannot be recommended, though doubtless within the next five years the chemists of the world will discover an oral contraceptive. *V. B. Green-Armytage*

454. **The Safe Period.**

By H. P. DUNN. *Lancet*, **2**, 441–442. Sept. 1, 1956. 1 table. 12 refs.

The author records the results of his survey of 156 patients using the "safe period" as a method of contraception. Fourteen days abstinence, i.e., 7 days before and 7 days after the calculated date of ovulation is practised. The total failure-rate of the method was 5·9 and the method failure-rate was 3·3 pregnancies per 100 woman-years. *H. H. Fouracre Barns*

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

455. **Cysts of the Vulvovaginal (Bartholin's) Gland.**

By M. L. TANCER, M. ROSENBERG and D. FERNANDEZ. *Obstet. Gynec.*, **7**, 608–610. June 1956. 5 refs.

Bartholin's cysts are due to cystic dilatation of the duct of Bartholin's gland. Treatment by enucleation can be time consuming and very haemorrhagic. The authors describe the result in 11 cases treated by marsupialization.

A linear incision is made in the overlying mucous membrane of the cyst just outside the hymen. The cyst cavity is opened and drained. An elliptical portion of the cyst lining is excised and a stoma is created 1–1·5 cm. in diameter. The edges of the cyst wall are everted and sutured to the surrounding skin and mucous membrane of the vestibule.

Stay in hospital for 1–2 days only is required. Six to 8 weeks later the stoma has contracted to a few millimetres in diameter. In all these cases and 11 further ones results were excellent. *J. G. Dumoulin*

456. **A Family History of Uterine and Gastro-intestinal Cancer.**

By D. SAVAGE. *Brit. med. J.*, **2**, 341–343. Aug. 11, 1956. 14 refs.

The author discusses previously recorded pedigree charts showing familial occurrence of uterine cancer. In such families the carcinoma was of the corpus, rather than the cervix. He describes a "Family N", in whom there are 19 members, comprising three generations. Twelve of these had confirmed cancers. Of the four male members one had cancer. Of the 15 female members, four had carcinoma of the uterus, one of the rectum, one of the stomach, and two surviving females had multiple primary cancers.

Eileen Wilson

457. **Role of Cytology in Detection of Carcinoma of Cervix.**

By R. E. L. NESBITT, Jr., and C. B. BRACK. *J. Amer. med. Ass.*, **161**, 183–188. May 19, 1956. 3 refs.

Cytology has assumed an important role in the detection of cancer, but there are still wide differences of opinion among gynaecologists as to its ultimate value in the diagnosis of uterine cancer. The vaginal smear is of limited value in the detection of endometrial cancer, and in cervical cancer it should be complementary to but not a replacement of histological techniques. Modern methods of cytological techniques are time-consuming and considerable experience is required in the interpretation of the morphological characteristics of the cells especially during pregnancy.

Working at the cancer detection clinic of the Johns Hopkins Hospital during the years 1947–1954 the authors studied the accuracy of diagnostic tests for carcinoma of the cervix in 5,617 women in whom cancer had not been previously diagnosed or treated. Of 310 proved cases of cervical cancer in this series 222 were correctly diagnosed by the initial smear. During the last year (1,019 cases) there was some improvement in diagnostic efficiency, but the absolute accuracy of the smear was still slightly below that of the biopsy. When however the pre-invasive lesions were considered separately the relative efficiency of the smear was greater in these than in the total group of cancer cases. The relative efficiency of the biopsy was not greatly different in the two groups.

The majority of advanced cases of cancer detected by the smear will be easily diagnosed by other procedures, but the greatest value of the smear lies in the detection of early cervical lesions and it should be used as a screening technique when the cervix is not grossly abnormal. Definitive diagnosis is never justified on the basis of one smear and multiple biopsies are frequently necessary before instituting definitive therapy.

D. W. James

458. **Results of Early Diagnosis of Cervical Carcinoma by Cytology and Colposcopy at the Gynaecological Department of the University Hospital in Graz, in 1954.** (Ergebnisse der Früherfassung des Collumcarcinoms mittels Cytologie und Kolposkopie an der Universitäts-Frauenklinik in Graz in 1954.)

By E. BURGHARDT and F. BAJARDI. *Arch. Gynäk.*, **187**, 621–637. 1956. 3 micrographs. 19 refs.

During 1954, 6,847 women were investigated by cervical smears and colposcopy. Of these patients 277 were suffering from cervical carcinoma and 169 had clinically manifest growths. There were positive or suspicious smears in 85·8 per cent, false negative reports due to screening errors in 1·2 per cent, true false negative smears in 3·6 per cent, and 9·5 per cent of the smears submitted were unsuitable for cytological examination. Of the 98 cases of pre-invasive malignancies 92·9 per cent had suspicious or positive reports, 3·1 per cent were false negatives due to screening errors and 7·1 per cent were true false negative readings. In roughly 40 per cent of the smears labelled "suspicious of malignancy" the patients were ultimately found to have pre-invasive cancer, whereas 92·0 per cent of all positive smears proved to be correct.

Of 7,803 colposcopic examinations in the same patients (103 cancer patients among them) 79 showed evidence of malignant disease. By colposcopy 78 per cent of the

pre-invasive lesions were diagnosed and 22 per cent were missed.

Comparing the results of these methods of investigation the authors point out that cytology has inherent errors (insufficient exfoliation and high degree of differentiation) as well as observer's errors. Colposcopy suffers from the same possibility of human error, as well as from the occasional uncharacteristic appearances of the lesion, and a lesion that is not situated within the observer's field of vision may be missed. The authors conclude that both methods are complementary and should be applied simultaneously. In the material presented reliance on colposcopy alone would have led to 12 cases of pre-invasive and 8 cases of early invasive cancers being missed; the sole use of cytology would have led to 5 pre-invasive and 2 early invasive cancers being missed.

E. Wachtel

459. **Cytochemical Observations on the Cells of Epithelioma of the Cervix Collected by the Method of Superficial Scraping.** (Osservazioni citochimische sulle cellule dell'epitelioma della portio prelevate per "abrasione superficiale".)

By P. SORA. *Ann. Ostet. Ginec.*, **77**, 1061–1068. Nov. 1955. 10 figs. 26 refs.

This represents the study by histochemical means of cells from epitheliomata of the vaginal portion of the cervix collected by the method of superficial scraping. These observations have been made on 16 cases. They have been studied by histochemical methods suitable for the demonstration of polysaccharides, lipoids, acid and alkaline phosphatase and cytochromic oxidase. Control cases from normal women were similarly stained.

It was found that glycogen was consistently absent from malignant cells. Staining for fat (Sudan B) gave a varied picture. In some cases numerous tiny fat granules were uniformly distributed in the cytoplasm, while in others these granules were less numerous but more abundant; a third appearance was the presence of large fatty inclusion droplets, obscuring the nucleus in some cases. These three appearances were often seen in the cells of the same preparation.

Alkaline phosphatase was always found in cancer cells. The reaction for acid phosphatase was always intensely positive.

A diminution in the quantity of cytochrome-oxidase was a uniform feature of malignant cells.

The absence of glycogen is attributed to the intense metabolic activity of the cancer cell which does not permit of storage. Variations in fat content are associated with the degree of metabolic activity at the time the cells were collected.

These methods are useful in studying the metabolic activity of cancer cells and have also a diagnostic value.

Josephine Barnes

460. **Endocervical Curettage.**

By L. CLARKE and H. L. GILMORE. *Obstet. Gynec.*, **7**, 634–645. June 1956. 23 refs.

Two hundred and forty-two cases of cervical carcinoma were seen at the Syracuse Memorial Hospital between 1949 and 1953. Only 70·8 per cent showed abnormal vaginal bleeding and in 25 per cent the cervix looked clinically normal. Thus, early cancer may be asymptomatic and show no visual evidence of disease. Papanicolaou smears were used but there are the snags of false positive and false negative results and the method does not reveal the geography of the growth. Similarly, cervical biopsy may miss early lesions. The authors therefore employed endocervical curettage with results considerably better than those obtained by biopsy in early cancer cases. The method was also more efficient than conization of the cervix in detecting cancer, and less cumbersome.

J. G. Dumoulin

461. **Hyperthecosis of the Ovary.** (Hyperthecosis ovarii.)

By W. P. PLATE. *Nederl. Tijdschr. Verlosk. Gynaek.*, **56**, 37–70. 1956. 5 figs. 133 refs.

The author reviews the histological findings in hyperthecosis of the ovaries, illustrating his points with photomicrographs from his own cases. The extensive literature on the symptomatology of the disease is considered in detail. The possibilities of the production of androgens in the normal ovary are examined and the role of luteinizing hormone in producing an imbalance of oestrogen and androgen is considered. The prolonged theoretical discussion and review of the literature (13 pages) is concluded by an analysis of 58 patients who had wedge resections of the ovary performed at the Utrecht Women's Clinic between 1949 and 1954. In 44 of these patients there was clear histological evidence of hyperthecosis. These cases are further analyzed in terms of the endometrial findings, symptomatology, hormone excretion and the effect of operation. It is concluded that the symptoms of Stein-Leventhal's syndrome show no clear correlation with ovarian hyperthecosis, nor is there any characteristic pattern of hormone excretion in patients suffering from hyperthecosis. The results of ovarian resection were very satisfactory in correcting menstrual irregularities, and poor in terms of hirsutism.

[A balanced review and a very modest and thorough analysis of one of the largest published series of cases of ovarian hyperthecosis.]

Arnold Klopper

462. **Ovarian Dysgerminoma: Operation: Radiotherapy: Eventual Pregnancy.** (Disgerminoma ovárico: operación: radioterapia: embarazo ulterior.)

By J. LEÓN and R. R. RODRIGUEZ PONTE. *Obstet. Ginec. lat-amer.*, **14**, 47–51. Feb. 1956. 2 photomicrographs.

The authors report a case of dysgerminoma in a single nulliparous young woman 19 years of age. The patient complained of abdominal pain, and on examination was found to have a hard mass rising out of the pelvis to the level of the umbilicus. Menses were normal. A provisional diagnosis of fibromyoma was made. At laparotomy, a right-sided freely mobile ovarian cyst

measuring 12 × 19 cm. was removed. It partly consisted of hard tissue and partly of semi-encysted fluid. On microscopical section, a diagnosis of dysgerminoma was made. Radiotherapy was prescribed, and because the capsule of the cyst was intact, the treatment was directed to the right side of the pelvis only. Except for a uterine haemorrhage shortly after the operation, four months amenorrhoea followed before the menses returned. Four-and-a-half years later, the patient married and had a normal pregnancy.

The authors conclude their report by discussing whether in such cases radiotherapy should be directed to both sides of the pelvis, which would permanently destroy the function of the other ovary rendering the patient sterile. Reviewing the literature, the authors cite 21 cases who received radiotherapy after operation, and of these 57·1 per cent were alive at the end of five years, as opposed to 41·7 per cent who did not receive any irradiation after the operation.

John F. Foulkes

463. **Endometrial Polyps.**

By W. F. PETERSON and E. R. NOVAK. *Obstet. Gynec.*, **8**, 40–49. July 1956. 8 figs. 5 tables. 21 refs.

A total of 1,100 cases of endometrial polyps has been studied by the authors at the Johns Hopkins Hospital embracing the years 1942–54. There was a wide variation in the ages of cases from 12 to 81 with a predilection for women in the middle years of life. In 18 per cent the women were menopausal and in 21 post-menopausal. In about 20 per cent of cases the polyps were multiple. Approximately 36 per cent of polyps showed changes compatible with the stage of the menstrual cycle. Of the immature, non-functioning polyps, some showed retrogressive hyperplasia of the lining epithelium with cystic dilatation, some had a metropathia "Swiss-cheese" endometrium and others showed an adenomatous or atypical hyperplasia.

In 43 per cent there were associated uterine myomas. In the menstrual era polyps were of little significance in so far as malignancy was concerned. In the post-menopausal woman this was not the case (10 per cent had endometrial cancer), although carcinomatous changes in a primarily benign polyp were seen in only 4 cases. It would seem that hyperplasia, polypoid or diffuse, should not be belittled if found in the post-menopausal era. Where there is an adenomatous pattern, or recurrence with increasing atypia in such cases, the likelihood of a malignant trend seems sufficiently great to make hysterectomy mandatory.

J. G. Dumoulin

464. **A Study of 531 Cases of Endometrial Carcinoma.**

By J. A. RANDALL and W. B. GODDARD. *Surg. Gynec. Obstet.*, **103**, 221–226. Aug. 1956. 9 figs. 10 refs.

The purpose of this article is to present a statistical analysis and summary of 531 cases of endometrial carcinoma admitted to the University of Iowa Hospitals during the years 1926 to 1951.

The average age at diagnosis was 59·2 years. Only 20 per cent of the patients were still menstruating, although 58 per cent menstruated beyond the age of 50 and can be considered to have had a late menopause. 25·9 per cent had never been pregnant. In 94·9 per cent the initial symptom was bleeding and in 3·4 per cent leucorrhoea was first noted.

The patients were divided into 4 clinical groups according to the stage of the disease and into 4 histological grades according to the degree of cell differentiation.

At the University Hospitals endometrial carcinomas have always been treated surgically if possible (60 per cent). Prior to 1935 hysterectomy alone or in combination with deep X-ray therapy was employed. Since 1935 it has been the policy to precede hysterectomy by an application of intra-cavitary radium. At first a tandem applicator was used, but since 1942 the procedure has been to pack the uterine cavity with multiple foci each containing 10 mg. of radium and filtered with 1 mm. of platinum. The radium was applied after diagnostic curettage and was left in place for three days. After 6 weeks hysterectomy was performed, steps being taken to prevent spill at the cervix or from the Fallopian tubes. A small number of technically operable cases were treated with radium alone or in combination with deep X-ray therapy, and patients with advanced carcinomas (Group 3 or 4) were usually treated with intra-uterine radium combined with X-ray therapy.

Of the 531 cases in the series, 516 were treated, with an apparent 5-year recovery rate of 53·6 per cent. Intracavitary radium followed by hysterectomy yielded better results than hysterectomy alone or in combination with X-ray therapy. Thus in the group of 194 treated by radium followed by hysterectomy there were 75·7 5-year survivals, while in the group treated by hysterectomy without intra-cavitary radium the 5-year survival rate was 55·8 per cent.

Multiple foci of radium proved more effective in sterilizing the uterine cavity of cancer, than 2 or more foci in a tandem applicator. Histological study of the uteri following hysterectomy revealed no residual carcinoma in 62·1 per cent of those treated by multiple foci but in only 33 per cent of those treated with the tandem applicator. The salvage of patients was roughly proportional to the number of complete sterilizations. The use of pre-operative intra-cavitary radium has eliminated recurrence in the vaginal vault.

Seventy-one patients were treated with intra-cavitary radium only, with a 5-year survival rate of 49·3 per cent.

The clinical stage of the carcinoma when treatment was undertaken proved an important factor in prognosis as did the histological grade. The salvage was usually proportional to the degree of cell differentiation.

John P. Erskine

465. **Superiority of Surgical Treatment of Endometrial Carcinoma.**

By J. C. SMITH. *J. Amer. med. Ass.*, **160**, 1460–1464. Apr. 28, 1956. 1 fig. 5 refs.

The "principle of treatment" of endometrial carcinoma is the eradication of all tumour cells from the largest amount of pelvic tissue at the earliest possible moment

after the diagnosis is established. In order to determine whether hysterectomy or radiation therapy clears the larger amount of pelvic tissue of cancer cells the author records data of six cases (from the Department of Pathology, St. Luke's Hospital, Saginaw) of endometrial carcinoma treated pre-operatively with radium therapy. In three of these six cases it was apparent on histological examination that all of the tumour cells had not been eradicated by the pre-operative radiation. The combined treatment ordinarily requires from four to eight weeks for completion, and during this time tumour cells beyond the range of radium may cause distant metastases. Primary hysterectomy therefore has advantages over the combined method.

Radium is also said to be useful in the control of infection, but antibiotics will control infection without risk to the patient, and the theory that radium prevents mestastases due to operative manipulation is difficult to prove.

Two tables are given to show the results of various authors. In the first table 706 cases treated by the combined method are compared with 649 cases in the second table treated by hysterectomy alone. In each group the five year survival rate is given and at first sight this appears to favour the combined method. The chief variable in the analysis however is that of tumour cell distribution and this is really the major determinant of survival rate. The final conclusion is that primary surgical treatment most nearly fulfils the objectives of the "principle of treatment" as originally defined by the author.

D. W. James

OPERATIONS

466. **Abdominal Colporrhaphy.**

By S. Sur Roy. *J. Obstet. Gynaec. India*, **6**, 395–398. June 1956. 1 ref.

Eight cases of abdominal colporrhaphy are recorded, together with the indications for the operation, and the technique employed. There are cases of prolapse associated with unhealthy pelvic organs, in which vaginal hysterectomy is not the treatment of choice. For example, the uterus may be too large for easy vaginal removal, or marked pelvic adhesions may be present. In such cases, the author usually does a sub-total hysterectomy by the abdominal route, followed by a vaginal repair operation. If removal of the whole uterus is indicated, however, he does a total hysterectomy followed by an abdominal anterior colporrhaphy, the posterior colporrhaphy being done vaginally.

The effectiveness of the operation is said to depend on the fact that the pubo-cervical fascia consists of 2 layers, a superficial layer running from the pubis to the supravaginal cervix, and a deep layer passing backwards and laterally to blend with Mackenrodt's ligament. If this is so, transverse shortening of the pubo-cervical fascia will cure a cystocele and support the vault of the vagina.

In performing a total hysterectomy, the bladder is separated from the vagina to a greater extent than is usual. The vessels and vaginal angles are tied, the sutures of the latter being left long. A triangular segment of anterior vaginal wall is excised, the apex being near the upper end of the urethra. The anterior vaginal wall edges are then approximated. The vaginal vault is closed transversely as usual. The vaginal angles are then tied to the round and utero-sacral ligament of the same side. The pelvic peritoneum is closed, and the posterior colporrhaphy is completed vaginally.

[This operation differs little from that originally described by Macleod (*J. Obstet. Gynaec. Brit. Emp.*, 1951, **58**, 583).]

John McKiddie

467. **Polyethylene Tubing in Salpingoplastic Operations.**

By P. T. Topkins, D. A. Frenkel and A. M. Siegler. *Fertil. Steril.*, **7**, 232–240. May/June 1956.

The authors describe an ingenious procedure which they have employed in cases where the fimbriated end has been pathologically destroyed, or in which the tube in its outer third has become blocked. [This is not the place minutely to describe the technique but the reviewer having done 3 of these operations can definitely state that any surgeon accustomed to this type of work will find it not too difficult.]

An incision is made on the anterior wall of the uterus into its cavity and then a fine probe is passed through the internal ostium of the tube out to the excised cuff-ended portion and then No. 1 size polythene tubing is threaded on to its end, and then slowly withdrawn until it reaches the endometrial cavity. In order to pass this thin polythene into the vagina it is necessary to pass down first a 6 inch length of No. 3 tubing through which the No. 1 is passed with ease and gently withdrawn as far as is needed. The authors do not seal off the ends but attach the polythene tubing to a rubber drip which runs continuously containing 5 per cent dextrose, 150 mg. cortisone and 10 million units of penicillin to the litre. This drip runs at the rate of 10–15 drops to the minute for the first 5 post-operative days and is intended to maintain patency and sterility of the traumatized area. The authors keep the polythene tubing in for 6–8 weeks and feel sure that there is less tendency for adhesions or adhesiveness of the tubal mucous membrane. However, they do not report any pregnancies up to date.

V. B. Green-Armytage

468. **Tubal Plastic Surgery.**

By A. M. Siegler and L. M. Hellman. *Fertil. Steril.*, **7**, 170–177. Mar./Apr. 1956.

Following the example of Greenhill in 1937, the authors sent a questionnaire to 4,910 Canadian and American gynaecologists who were interested in tubal surgery, and they received 734 replies, which is a 15 per cent response! Fifty per cent of the surgeons stated that they never did plastic operations on Fallopian tubes for the correction of tubal occlusion, and 39 per cent had performed less than 10 tubal plastic operations; whereas only 11 per cent had done 10 or more such operations. It would appear that the pregnancy rate for salpingolysis was 24 per cent; whereas for salpingostomy (cuff operation) the conception rate was 20·3 per cent,

though in each of these types of surgery there was an incidence of 7·3 and 12 per cent of ectopic pregnancy. Tubal implantation was done by 51 of the replying surgeons with a total pregnancy rate of 26 per cent, though 9·2 per cent were ectopic pregnancies. [It would seem that in evaluating the surgery of implantation that the authors have taken no heed as to the pathological type, for it is obvious that if the tubes have been affected by pathogenic organisms throughout their length that the prognosis of any surgery must be poor, indeed so poor as to contra-indicate any operation. But if surgeons would strictly restrict operation to (1) cases where the tubal fimbriae are only enfolded, the so-called phimotic tube or (2) those cases where the intimate history denotes that there has been an abortion often induced or criminal, or curettage, placenta praevia or Caesarean section, all conditions which entail the risk of streptococcal infection of the secundines with cornual occlusion rarely spreading beyond the isthmus, then the surgical results of tubo-uterine implantation in America and Canada would equate with those in Paris and London where full term pregnancy, with or without Caesarean section, has occurred in 39–41 per cent of all cases operated upon. It is to be hoped that in any future questionnaire that the authors of this extremely interesting paper will especially demand attention to the type of patient and type of pathological occlusion that exists before operation, so that successful results can be assessed more readily.]

V. B. Green-Armytage

469. **Stress Incontinence Following the Manchester Operation for Prolapse.**

By C.-O. Danielsson, C. Franksson and I. Petersen. *Acta obstet. gynec. scand.*, **35**, 337–344. 1956. 3 figs. 10 refs.

The authors, writing from Stockholm hospitals, investigated the cause of stress incontinence in 12 patients, aged between 35 and 75 years, who had undergone Manchester type repairs for prolapse. Eight of them had stress incontinence before the operation, 4 developed the condition after the operation. The methods used were vaginal examination, urinanalysis, urography, urethrocystography, urethrocystoscopy, cystometry, and electromyographic examination of the striated urethral sphincter and the pubococcygeus muscle. In the latter method, electrodes are inserted into the respective muscles, and the action potentials are recorded with a cathode ray oscillograph.

Vaginal examination showed one "major recurrence with cystocele and prolapse of the uterus", and 4 "minor cystoceles"; in the remainder the anatomical results of the operation were good. In a few cases, urethrocystoscopy revealed some deformity of the urethra probably due to cicatrization. The other investigations, apart from electromyography, showed no abnormalities.

In none of the 12 cases did electromyographic examination of the striated urethral sphincter disclose any electric activity in its dorsal part nearest the vagina; this is a regular finding in women who have borne children and denotes a defect in the sphincter muscle. In 9 cases the electromyograms were suggestive of similar defects in other parts of the sphincter as well. In 4 patients an electromyographic pattern characteristic of a lesion of the peripheral motor neurone supplying the muscle was shown. All but one patient exhibited normal electromyograms from the levatores ani.

It is concluded that both birth trauma and operative trauma during dissection may be responsible for either injury to the nerves supplying the levatores and the urethral sphincter, or for scar formation in the muscle, or for both these lesions.

[These interesting findings would be convincing if normal electromyographic patterns had been obtained from the whole urethral sphincter in cases of functionally successful repair operations.] *N. Alders*

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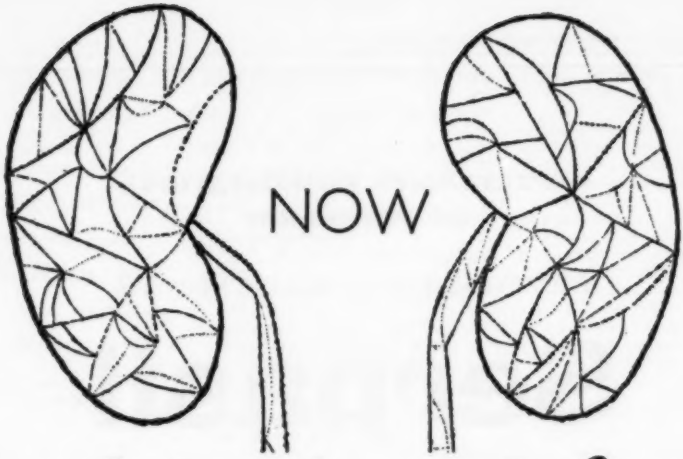

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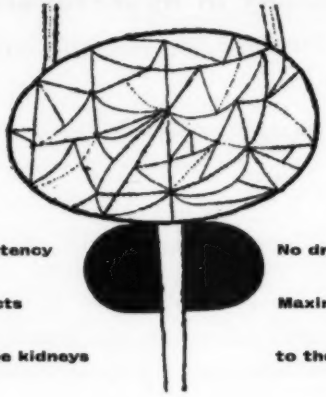

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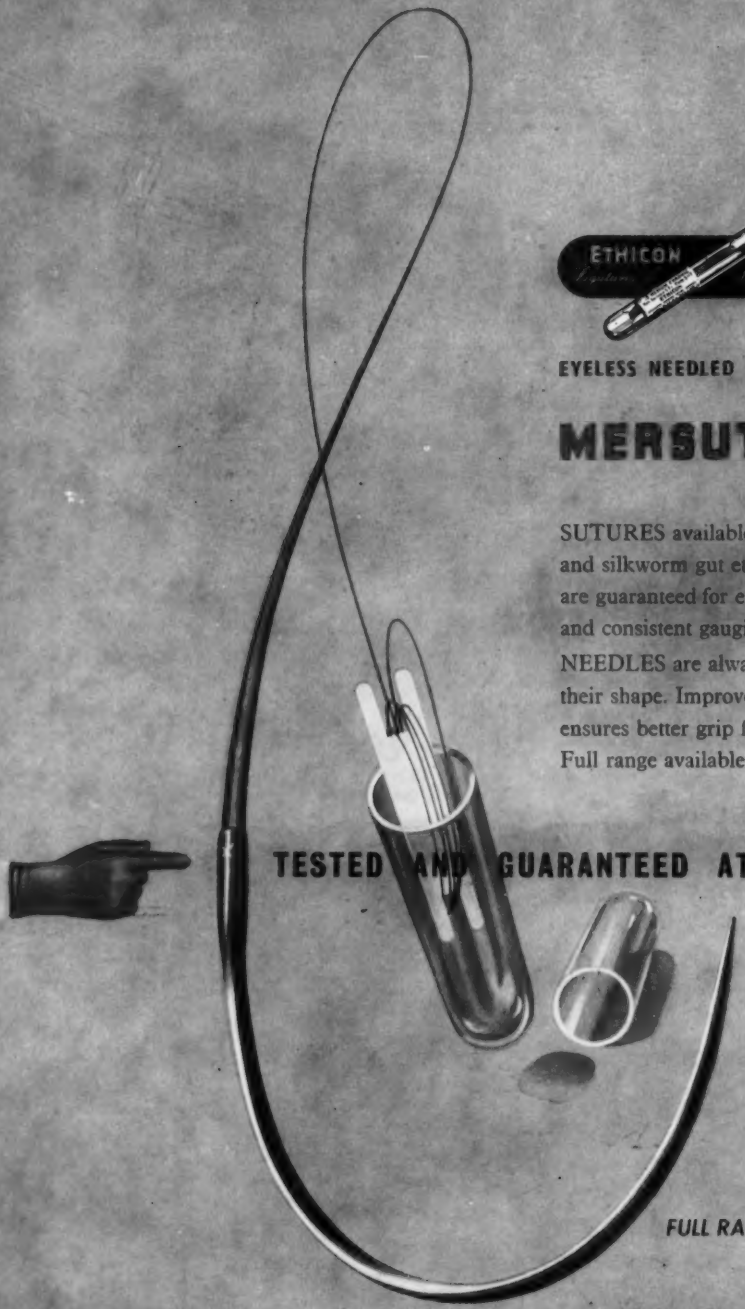

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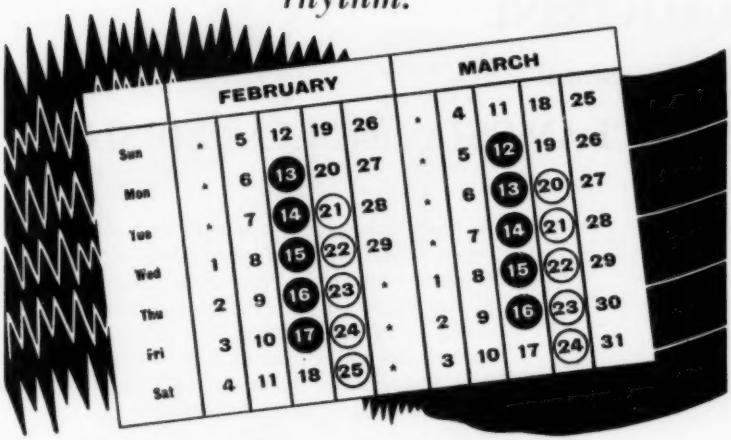

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1. *Wis. med. J.* (1954) 53:322.
2. *Amer. J. Obstet. Gynec.* (1954) 3:201.
3. *J. Indiana med. Ass.* (1954) 47:869
4. *J. Clin. Endocr.* (1954) 14:272.

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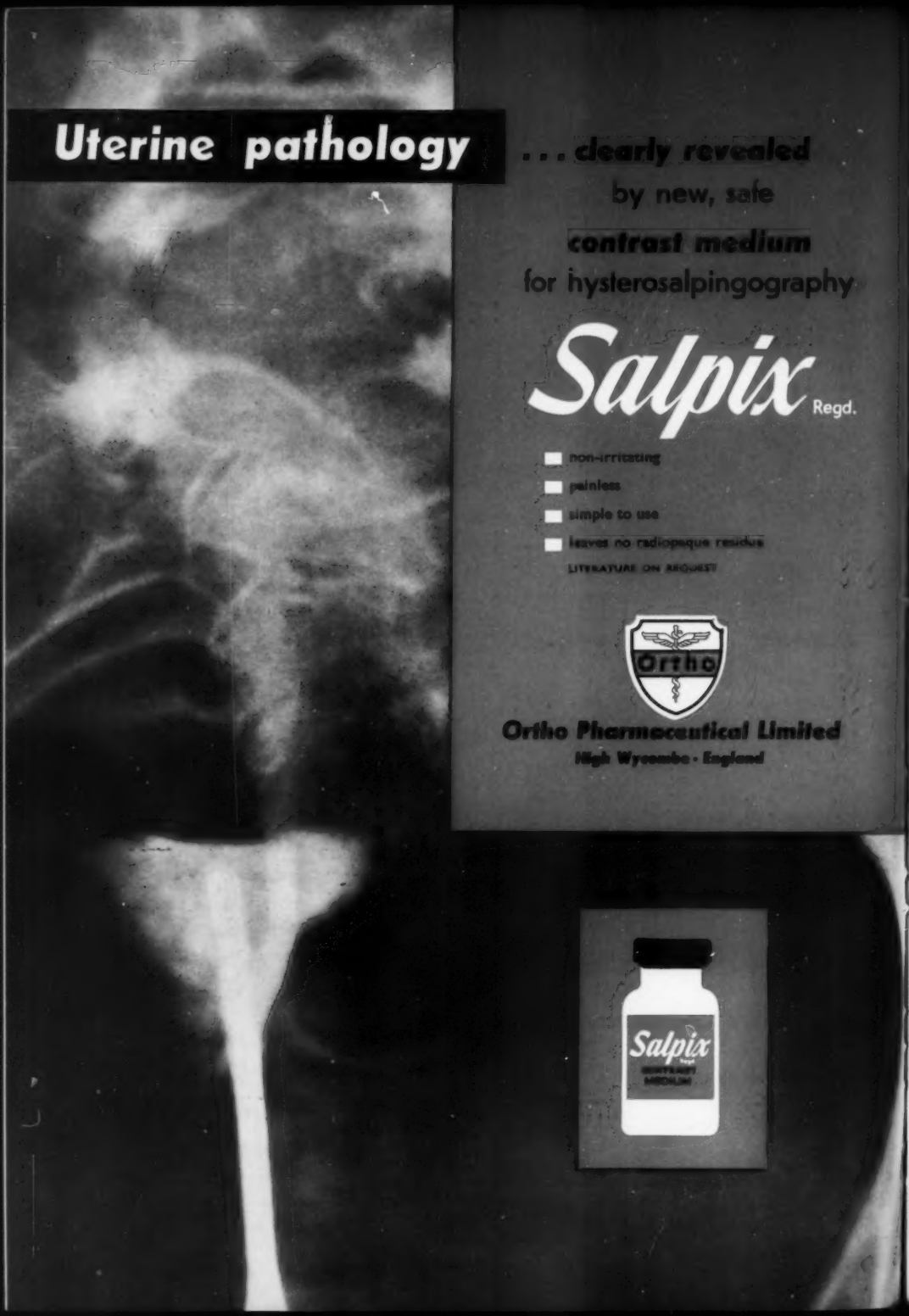
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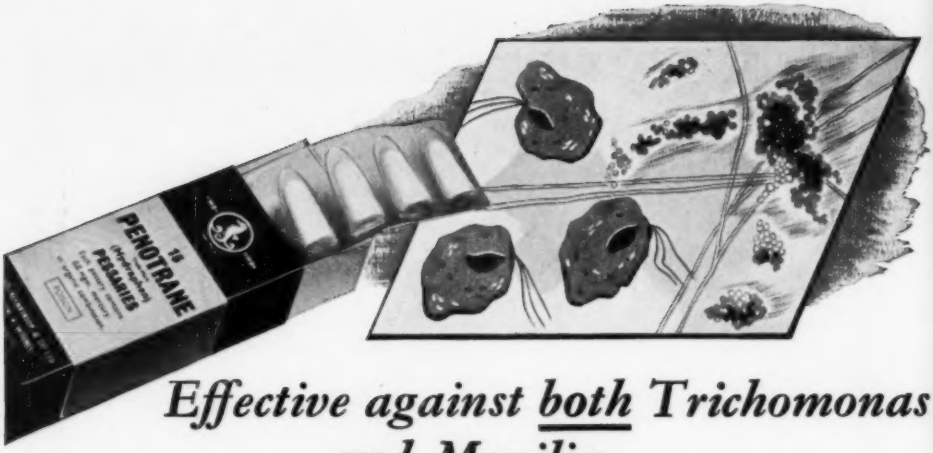

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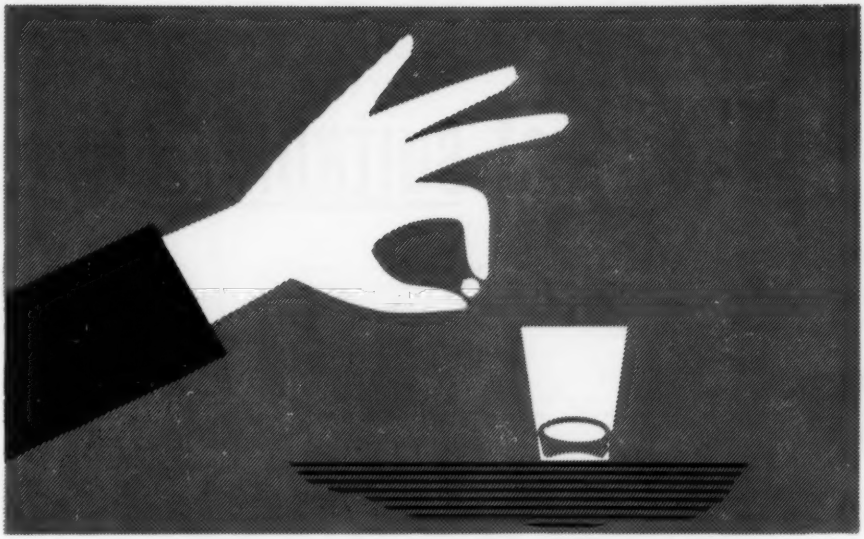

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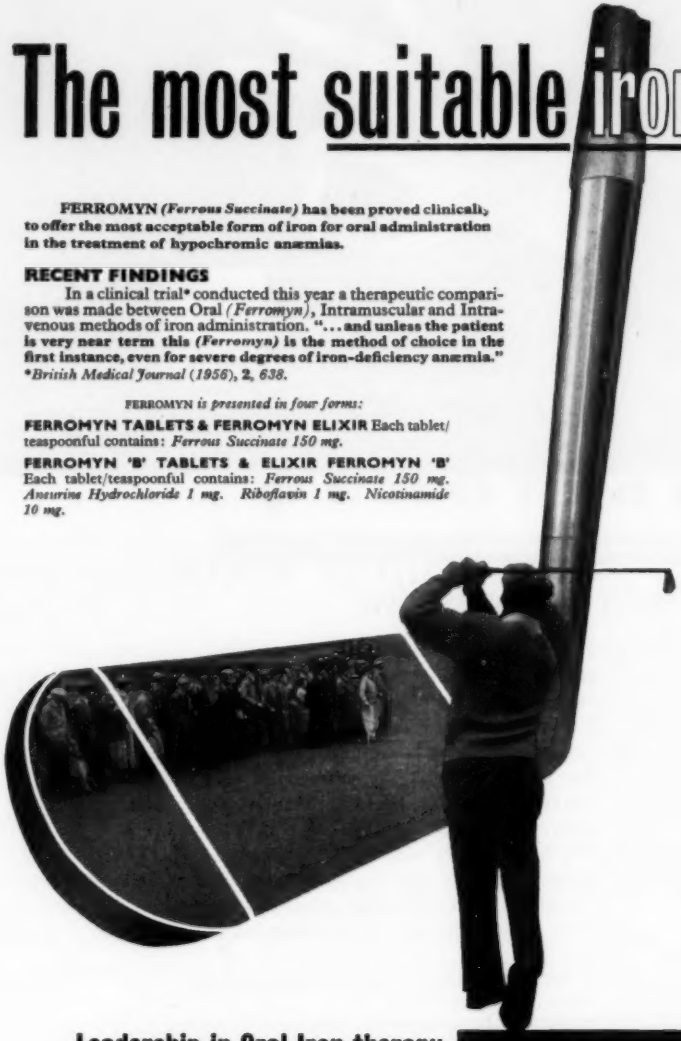

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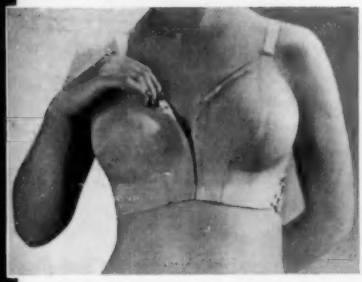

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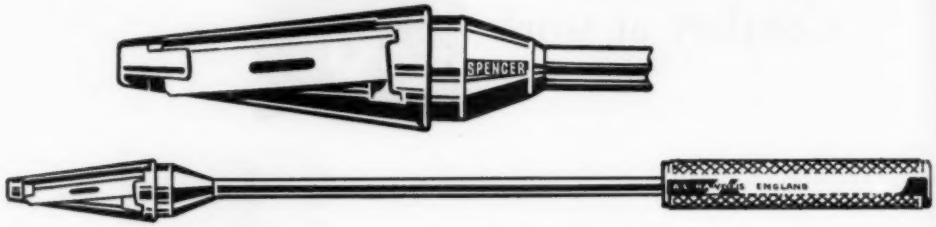

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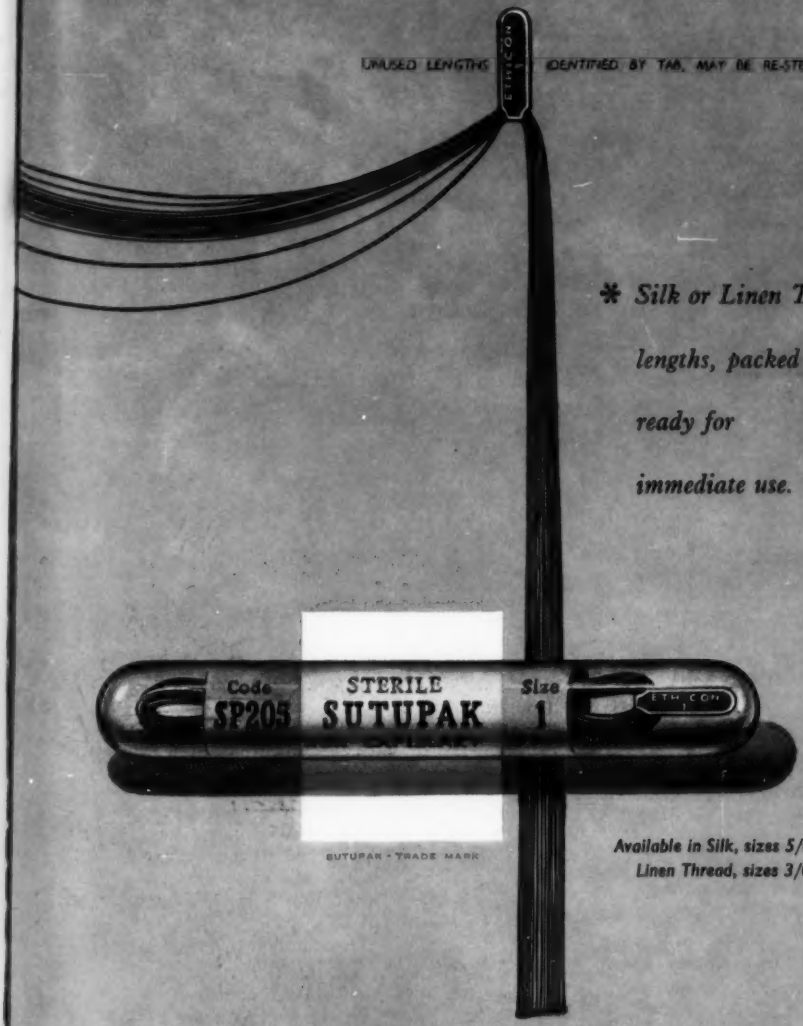

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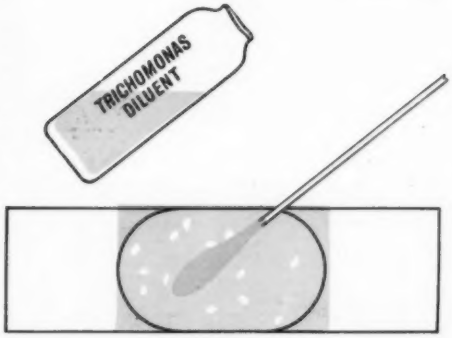

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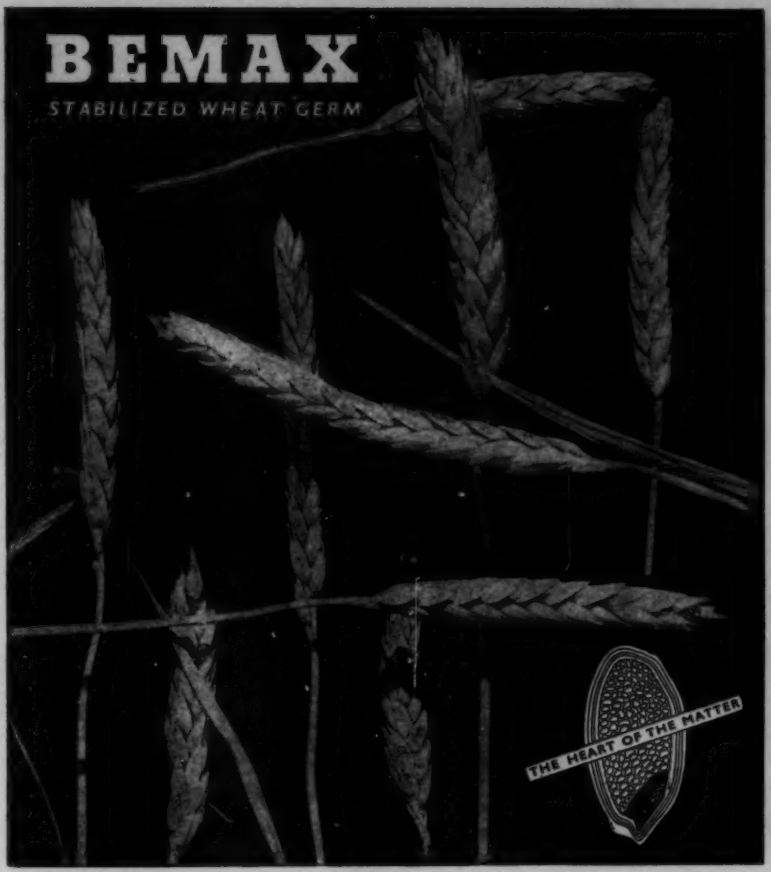

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